UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM Date: January 24, 2001

SUBJECT: Atrazine: Response to Syngenta's Comments on the EPA's November 30, 2000 Draft "Atrazine: HED's Preliminary Human Health Risk Assessment (and Associated EPA Documents) for the Reregistration Eligibility Decision (RED). Chemical Number 080803.
DP Barcode D272111

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TO: Pam Noyes, Chemical Review Manager
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Please find attached a response to Syngenta's "Comments on the EPA's November 30, 2000 Draft "Atrazine: HED's Preliminary Human Health Risk Assessment (and Associated EPA Documents) for the Reregistration Eligibility Decision (RED)".

HED responsers were Catherine Eiden, Linda Taylor, Vicki Dellarco, Gary Bangs and David Soderberg. David Widawsky responded for BEAD. Mary Frankenberry and James Lin responded for EFED.

Syngenta's Comments on the EPA's November 30, 2000 Draft "Atrazine: HED's Preliminary Human Health Risk Assessment (and Associated EPA Documents) for the Reregistration Eligibility Decision (RED)

I. Introduction/Background

Syngenta Crop Protection, Inc. (formerly Novartis Crop Protection, Inc.) appreciates the opportunity to provide comments on the draft documents provided by the EPA in the letter to Janis McFarland dated December 1, 2000 (received by Syngenta on December 2, 2000) in advance of their formal publication for public comment.

Atrazine has been an important weed control tool for American farmers for over 40 years, and continues to be the chemical of choice for use in reduced tillage systems for corn and sorghum. Syngenta is committed to providing comprehensive toxicology and exposure data important to assess human risks associated with atrazine exposure through the diet, water, and as a result of occupational and residential exposures. The comments in this document, while focusing on errors as requested by the Agency, also address methodology questions.

The comments have been organized according to the structure provided in EPA's draft RED such that the basic preliminary human health risk assessment and each of the associated EPA documents are discussed separately. A separate section for labeling and product usage information errors in all documents were summarized in a separate document by section. Also, at the request of the Agency, we are providing a listing of additional ongoing research and/or documents on a variety of topics, along with projected dates for their submission to the Agency. A probabilistic assessment of drinking water and diet combined is included with this response.

II. Executive Summary

The following sections provide Syngenta's comments on EPA's preliminary findings and conclusions. We are providing these inputs to EPA in order to develop the most scientifically valid risk evaluation for atrazine.

A. Drinking Water (Deterministic)

- Aerobic soil half-life: The most appropriate mean aerobic soil metabolism half-life value is 61 days as reported by the Atrazine Ecological Risk Assessment Panel in their Expert Panel Report (final report to be submitted to EPA as part of the Syngenta response to the Preliminary Environmental Fate and Effects Risk Assessment) should be used in the preliminary risk assessment.

EFED Response:

A detailed evaluation of data considered by EFED, including aerobic soil metabolism data, is presented in the Environmental Fate & Effects Chapter, which was submitted one week following submission of the DW Assessment. EFED will review any additional studies Syngenta sends.

‘ Regression equations: Syngenta used a more robust set of water data, which included both raw and finished water, as opposed to finished water only, to more accurately develop seasonal regression equations to calculate total chloro residues from measured atrazine concentrations.

EFED Response:

We do not know the exact numbers of CWSs that did not treat their water. Considering that most of the CWSs are treating their water, it would be a better representation to derive the regression equations based on the finished water only. Therefore, the finished water values are used in the risk assessment.

‘ Time weighted means: The preliminary risk assessment did not use estimates of annual and seasonal (3-month) means with the time-weighted process for the Community Water Systems (CWS) from the three databases used in the preliminary risk assessment. This results in an over or under estimation of the total chloro-triazine CWS annual and seasonal means. The time-weighted procedure is required for the monitoring data in the Syngenta Voluntary Monitoring Program (referred to as VMS) and the Acetochlor Registration Partnership (ARP) databases due to the increased number of samples per year with a greater number of samples subsequent to the atrazine application period (May–July).

EFED Response:

There are some differences in using the simple average versus the time weighted average. The concentration values of parent atrazine for VMS and ARP presented in EFED’s assessment are based on the time weighted average approach. To be consistent, EFED has modified the values of total chloro-triazines by using the time weighted average approach for the annual mean.

Both VMS and ARP were sampled either weekly or bi-weekly during the use season, and sampled monthly other seasons. With the constant weekly or bi-weekly sampling, there will be little difference between the seasonal mean calculated by simple averaging and the time weighted seasonal mean. For the seasonal mean, EFED has done some preliminary comparisons on a few CWSs and found that the difference is not significant, with some arithmetic means being higher than their time weighted counterparts and some being lower. EFED will consider further re-

calculation of time weighted seasonal means for the rest of the data in the next draft.

‘ Composite water database: The various databases (PLEX, ARP, VMS) should be combined prior to calculating seasonal and annual means. Time weighting rather than simple averaging results in a statistically stronger and more accurate data set for analysis of likely exposures.

EFED Response:

Ideally, to pool the different data sets, the study designs should be identical. Since EFED is not certain that all the controlled factors are identical for these thee data sets, it is possible that there are some design differences. The differences exist in (1) the number of sampled CWSs, (2) the sampling dates, and (3) the detection limits. If all three data sets were compatible, results from all the CWSs should be combined and not just those from the selected few. EFED therefore believes that the datasets should not be pooled.

‘ Exposure period: Since these data sets span several years, time weighted means covering the same exposure duration as that being assessed in each exposure scenario should be determined (i.e. a seasonal mean should not be compared to a DWLOC for chronic exposure).

HED Response:

Comparison of seasonal mean concentrations (based on average residues of atrazine and the chlorinated metabolites over 3 months as estimated from the VMS and ARP databases) to chronic DWLOC values is considered appropriate to estimate risk for intermediate-term to chronic effects because the selected effect (the attenuation of the LH surge as a biomarker indicative of atrazine’s ability to alter hypothalamic-pituitary function in general) occurs between 30 days to 5 months of daily exposure depending on the dose levels used in the animal studies. The exposure period of interest for atrazine residues in CWS using surface water in the Midwest is during the spring shortly after application.

‘ Chronic drinking water exposure: The number of CWS exceeding the proposed chronic DWLOC of infants (12.5 ppb) in Tables 10, 11, 13, 14 for annual and seasonal total chloro triazine means should be reexamined with the proper time-weighted calculation of mean exposure for each time period. In addition, the total chloro triazine period mean concentration for each of the CWS in the three databases should be incorporated into the assessment. The period mean exposure concentration (based on an average of annual means for the number of consecutive years monitored) is the most accurate estimation of chronic exposure to the eight population subgroups. These data should be included to better and

more accurately evaluate the CWS exposure profile for each of the population subgroups chronic DWLOC values.

HED Response:

EFED recalculated time-weighted mean concentrations (TMMC) for CWS using surface water in PLEX, ARP, and VMS. HED has reexamined the TWMC for comparison to DWLOC values, and incorporated the changes into the risk assessment. HED will consider inclusion of the period mean into the risk assessment in subsequrnt revisions to the risk assessment. However, HED notes that the period of interest for intermediate-term to chronic drinking water exposures to atrazine residues is the seasonal pulses that occur shortly after application in the Spring.

‘ Novartis Rural Well Survey: The data from this rural well survey represent rare, worst case high-end exposure scenarios because these wells were selected based on previous detections of atrazine and/or are located in high atrazine use areas where ground water is hydrogeologically vulnerable. Thus, the Novartis rural well data are generally not appropriate for a regional/national scale population-based exposure assessment, and these findings should only be used for local best management practice efforts to reduce exposures.

HED Response:

The risk assessment now includes language addressing the high-end and targeted nature of the exposures estimated from the Novartis Rural Well Survey.

‘ Point source contamination: Eight wells (out of 1,505 wells sampled in the Novartis Rural Well Survey) had atrazine concentrations exceeding the MCL of 3 :g/L. Based on follow-up investigations, point source contamination rather than labeled use contributed to the detection of relatively high atrazine concentrations in at least 3 of these wells.

EFED Response:

EFED stated in the drinking water memo that the Rural Well Survey is likely to have the most negative bias due to inadequate sampling frequency (only one sample per well). As the ARP groundwater monitoring results, showing that the monthly variation can be significant, which has relevance for the uncertainty in the results of the rural well study. Additional information on any of the eight wells with residue levels of concern is welcomed, particulary additional monitoring in those wells.

‘ ARP data: Table 8-1 provided percentile values of atrazine in ground water based on an ARP Groundwater Monitoring Study for the period from May 1995 to March

1998. The numbers could not be verified for accuracy because Syngenta does not have access to the ARP groundwater data.

HED Response:

HED encourages the registrant to request these data relevant to atrazine from the ARP.

- National Alachlor Well Water Survey: Results from this survey (Holden and Graham et. al., Environ. Sci. Technol., Vol. 26, No. 5, 1992) indicate that the MCL exceedance frequency of atrazine in private, rural domestic wells was less than 0.1% which is more than 5 times lower than the results from the Novartis Rural Well Study (i.e. 0.5%). Additional information on atrazine detection in rural non-community system wells in 21 major atrazine use states was included in the PLEX Update IV (Submitted to EPA in June 1998 MRID 44597601). The data indicated that atrazine was detected above 3.0 ppb in 0.15% of private rural wells (25 out of 16,382 rural wells) which is very similar to the results from the National Alachlor Well Water Survey. As noted above, the Novartis rural well survey was not designed to be used for predictions of concentrations of atrazine in regions or sub-populations.

EFED Response:

PLEX IV estimates a population of 15-17 million residing in these 21 states was not served by CWS and presumed this population is served by individual wells. According to the PLEX IV, the mean atrazine concentration of 0.154 ppb for 11,122 CWSs from groundwater in 17 major use states is higher than the mean atrazine concentration for rural wells from all of the four multi-state studies. The rural well studies have mean atrazine concentrations of 0.152 ppb (Novartis Rural Well Study), 0.058 ppb (USGS/NAWQA Study), 0.037 ppb (USGS/Mid-continent Study) and 0.057 ppb (Farm Bureau/Heidleburg College Study) based on the respective number of major use states monitored in each study. Since the mean concentration of atrazine for the Novartis Rural Well Study is compatible with the mean of 11,122 CWS of groundwater source, the risk assessment results based on the rural well study for the groundwater drinking water source should be applicable to the 11,122 CWSs in 17 major use states from groundwater sources.

B. Occupational Mixer/Loader/Applicator

- Exposure scenarios: Several scenarios do not exist and should be deleted (pp. 15 &16 of the Occupational and Residential Exposure Assessment and Recommendations for the RED). These scenarios include (1c), (1e), (2c), 3, 6, 9, and 15. Syngenta will be providing a document that will describe the possible exposure scenarios more accurately than is depicted in this document.

HED Response:

These are "right-of-way" exposure scenarios. The labels for this use do not clearly limit application to “roadsides” but instead “highway rights-of-way.” There is no application equipment specified on the labels, so HED has used the closest equipment for which surrogate exposure data are available, which is commonly called the “right-of-way sprayer.” There is little data on the equipment used or exposure information, so this is a best-estimate based on HED and BEAD experience. The labeled rates include, 1, 2, 2.2, and 4 lbs ai/acre and all are special local need (SLN) registrations. The 4 lbs ai/acre labels are still active but are dated 1985 and 1989. The Chemical Review Manager for atrazine is currently attempting to determine the need for continued registration of these SLN registrations, particularly at the higher application rates.

‘ Aerial: Information from university experts indicate that this is a limited market, particularly in conifer forests and Christmas tree farms. Because of the nature of the terrain in these farms, helicopters must be used. With relatively small forestry sites and changing wind conditions, the practical range of treated acres per day is 150-350 acres, not the 1200 acres listed. Furthermore, applications take place in the course of a week, entailing only a short-term (and not intermediate-term) exposure. Only short-term risks should be calculated.

HED Response:

The daily acreage treated for conifer forests has been revised to a reasonable high daily limit of 350 acres, and the risk assessment has been changed to reflect this number. The Syngenta information is welcomed, and confirmed by a range of 67-343 acres as “typical to high” from surveys by NAAA (data supplied electronically by the NAAA on January 2-4, 2000). The Agency is seeking further information from all sources, including the USDA Forest Service.

‘ Bulk fertilizer: "On-farm" preparation is not done. Fertilizer pre-mixing is done in automated large-scale blenders. In addition, the assumption that 960 tons of fertilizer is mixed and loaded is not correct. The actual amount is more likely to be 150 - 300 tons. Syngenta will be submitting a document that will more fully describe the treatment process, possible exposure scenarios, and risk calculations.

HED Response:

The Agency encourages submission of additional information to clarify this exposure scenario. The Agency believes, at a minimum, individual farmers may apply treated fertilizer, and encourages submission of information about daily acres fertilized and equipment used.

‘ Rights-of-way: Syngenta atrazine formulations are not used on rights-of-way areas (this use is not supported by Syngenta), but are used on roadsides. AAtrex

products are used at a rate of 1 lb. a.i./acre for roadsides, and not 4 lbs. ai/acre rate as noted in the document.

HED Response:

The labels for this use do not clearly limit application to “roadsides” but instead “highway rights-of-way.” There is no application equipment specified on the labels, so HED has used the closest equipment for which surrogate exposure data are available, which is commonly called the “right-of-way sprayer.” There is little data on the equipment used or exposure information, so this is a best-estimate based on HED and BEAD experience. The labeled rates include, 1, 2, 2.2, and 4 lbs ai/acre and all are special local need (SLN) registrations. The 4 lbs ai/acre labels are still active but are dated 1985 and 1989. The Chemical Review Manager for atrazine is currently attempting to determine the need for continued registration of these SLN registrations, particularly at the higher application rates.

‘ Flaggers: University experts and commercial applicators have verified that flaggers are no longer used. GPS is the method of choice to mark aerial application areas.

HED Response:

The revised preliminary risk assessment assumes that human flaggers will not be used when treating very large acreage, and there are no risk estimates of concern for flaggers. The Agency agrees that most aircraft used for aerial application are now equipped with GPS or other means to determine the area to spray, and what has already been sprayed. The NAAA 1998 survey indicates about 60% of aerial applicators use a GPS control system, and 85% use some mechanical or electronic control system (only 15% use human flaggers). The survey shows that flaggers are still used in some instances and by some aerial applicators, predominantly pilot owner-operators . Atrazine labeling could stipulate use of GPS systems to eliminate hazards to human flaggers.

C. Occupational Post-Application

‘ A post-application exposure assessment is not required for fallow ground, roadsides, and conifer forests. Manual irrigating/moving of irrigation pipe and scouting are highly unlikely to occur in areas designated as fallow and roadsides (note rate should be 1 lb a.i./A). Manual irrigation/moving of irrigation pipe does not occur in newly planted conifer forests; scouting in conifer forests is not a typical practice.

‘ The risk assessment for people staking, topping, training or harvesting Christmas trees should be removed since there would be no atrazine residues at this time (3 or 9 months after application).

‘ The risk assessments for transplanting, harvesting and hand weeding golf course turf and sod farms should be removed. Treatment with atrazine to control weed growth is not followed by weeding on the day of application.

HED Response:

Based on comments received and confirmed by BEAD and other authorities on agriculture, postapplication exposure to atrazine on fallow lands or CRP grasslands is considered unlikely, and even less likely in the short-term after spraying. Exposure of workers on treated highway rights-of-way or roadsides would probably be unlikely in the first week after spraying, but it is possible the public could be exposed for short durations. The Agency has no transfer coefficients specific for tractor mowing. As a whole, these exposures are considered to be negligible. The BEAD also agrees that hand weeding sod or turf is unlikely at any time, and harvesting unlikely in the short term after herbicide application. Irrigation of forests or tree farms is unlikely, but staking may be done at any time. The exposure and risk assessment has been updated to reflect these refinements.

D. Residential Handler

‘ Both the low-pressure hand wand and hose-end sprayer application scenarios should be deleted. Neither of these techniques are practical application methods for a 1/2 acre (21,780 ft^2) lawn.

HED Response:

The use of 1000 sq ft for residential applicators using belly grinders is assumed, and use of a hand-wand for “spot treatment” would be limited to the same area. The revised exposure and risk assessment uses 1000 sq ft for the backpack and hand wand application by residents, assuming spot treatment use is more typical for these methods. Additional usage data, such as gallons used or acreage treated per day, could refine the current daily use rate assumptions and affect total exposure estimates. The Agency uses the Residential SOPs as the source for residential acreages applied, unless more specific information is available. The median lawn size is approximately 0.3 acres, while 0.5 acres is approximately the 80^{th} -90^{th} percentile, depending on the survey cited. Label instructions limiting use of the liquid formulation to spot-treatment would also help reduce the risk for low-pressure handwand and hose-end sprays as they would not be intended for application to an entire lawn.

‘ The central tendency, rather than the highest values, should be used for each data set.

HED Response:

The Agency has presented the MOEs using the average residues on each day after treatment, from each geographic application site. This provides the maximum amount of information for the Risk Manager for this chemical. For the purposes of regulation, i.e., labeling, sometimes residues will be averaged from different test sites if there are not significant differences in initial dislodgeable residue levels or rates of dissipation. The atrazine residue data show considerable geographic variation, particularly in dissipation rate. For both the liquid and granular applications on turf, the DFR dissipation rates were considerably slower at the Georgia site. The exposure duration can be an under- or over-estimate depending on the crop, location, time of year, i.e. scouting vs. harvesting, so for large assessments such as this the Agency uses eight hours consistently. The transfer coefficients for each activity for each crop incorporate the ARTF study data received to date, and the values are selected to be central tendency from the full range of the relevant studies.

‘ Only short-term risks need to be calculated. Intermediate-term risks are not likely.

HED Response:

The Agency recently revised the toxicity endpoint selection document for atrazine (HIARC Report 12/22/2000). In it, the Agency applies a short-term exposure duration of 1-30 days based on the length of time to the effects seen in both oral and dermal toxicity studies selected for short- and intermediate term exposures. Therefore, as was stated in the November 15, 2000 occupational and residential exposure assessment, most atrazine handler and all residential exposures are expected to be short-term in duration. For intermediate-term postapplication exposures, it is expected that no individual would consistently be exposed to average residues greater than those at DAT 7 for over 30 days. The text and tables have been revised to clarify this position.

E. Residential Re-Entry: Ingestion

‘ Sticky hand-to-mouth: This scenario has not been adequately peer reviewed and should not be included in any assessment until properly vetted and discussed and data availability and needs are understood. Nonetheless, in the interest of presenting a calculation of this type of scenario, the default 5% transfer rate should be replaced by the actual turf dislodgeable residue data for atrazine. Furthermore, a 3-fold increase in wet- versus dry-hand transfer should be used.

HED Response:

This is a policy issue and not an error, per se.

‘ Granule ingestion: There are no granular atrazine alone products, but only atrazine-treated fertilizer. Along with its small particle size, fertilizer may be caustic and is highly unlikely to be ingested.

HED Response:

Comment noted.

F. Residue Chemistry and Tolerance Reassessment

· Hydroxy atrazine tolerances: Only hydroxy atrazine (G-34048) and desethylhydroxy atrazine (GS-17794) should be included in the tolerance expression for hydroxy triazines because the other hydroxy triazines are very minor components in the crop metabolic profiles.

HED Response:

If the registrant can demonstrate through available data that the only hydroxy compounds of concern, i.e., detected in significant quantities, are the hydroxy atrazine (G-34048) and desethyl hydroxy atrazine (GS-17794), EPA will reconsider the requirement for establishing a tolerance on all four hydroxy compounds and a supporting analytical method. Based on our brief review of the residue data for the hydroxy compounds from available metabolism studies, hydroxy atrazine (G-34048) and desethyl hydroxy atrazine (GS-17794) are all detected in plant commodities; however, the des isopropyl hydroxy atrazine compound has also been detected in metabolism studies.

· Wheat hay: In a 1995 EPA memorandum, the Agency recommended that a radiolabeled field residue study in fallow/wheat would satisfy the magnitude of the residue requirement for wheat. Therefore a full geography wheat hay study should not be required.

HED Response:

HED has reevaluated the need for geographically representative studies in wheat hay in response to this comment. Residues of atrazine in wheat forage, the wheat commodity with the highest residues, were up to 1.11 ppm, yielding a tolerance of 1.5 ppm in wheat forage. HED believes that a tolerance in wheat hay can be supported using the residues in wheat forage corrected for percent dry matter. Correcting 1.11 ppm for the ratio of percent dry matter between wheat forage and wheat hay (Hay/Forage = 88%/25% = 3.5), yields estimated residues in wheat hay at 3.9 ppm. From this HED proposes a tolerance in wheat hay at 5 ppm. If the registrant disagrees with this proposed tolerance, geographically representative studies must be submitted to support a different tolerance.

A tolerance for the hydroxy metabolites on wheat hay is also required. HED has proposed a reassessed tolerance for the hydroxy metabolites of atrazine on wheat forage at 0.5 ppm based on existing field trial data. HED further proposes a wheat hay tolerance for the hydroxy metabolites of atrazine of 1.5 ppm. The registrant may otherwise submit field trial data for establishing tolerance level residues for the hydroxy metabolites of atrazine on wheat hay.

- Milk tolerance: According to all available data, the milk tolerance should remain at 0.02 ppm.

HED Response:

The reassessed milk tolerance of 0.10 ppm is based on combined residues of atrazine and the chlorinated metabolites taken from an anmal feeding study in which milk was sampled and analyzed for atrazine and all of the chlorinated metabolites. The summed residues were <0.06 ppm based on detectable residues of diaminochlorotriazine (DACT) in milk samples at up to 0.03 ppm and residues of atrazine and desethyl atrazine and desisopropyl atrazine at the detection limit (<0.01 ppm) each from dairy cows fed atrazine at a 3.75 ppm feeding level. The theoretical maximum dietary burden (MTDB) for atrazine in the dairy cattle diet (based on tolerance level residues) is 5 ppm.. The ratio of the MTDB to the feeding level closest to the MTDB used in the animal feeding study is 1.3X. Residues of <0.06 ppm multiplied by 1.3X approximate <0.08 ppm, which has been rounded to 0.1 ppm for the tolerance level for residues of atrazine and the chlorinated metabolites in milk.

The tolerance in milk is set as an upper bound on legal residues in milk. It is based on residues detected from animal feeding studies and the maximum theoretical dietary burden for atrazine in the diets of dairy cattle. It is not based on actual monitoring data or anticipated residues as are used in the dietary exposure assessments. Necessarily, the tolerance is higher than any anticipated residues of atrazine in milk.

- Percent crop treated: High values (in some cases implausible) are assigned for percent crop treated, e.g. 97% corn and 100% sorghum treated. Also, information was not given on data sources nor was a rationale given for the weighting procedure for estimating usage.

HED Response:

BEAD has revised the usage estimates on corn and the revised estimates have been incorporated into a revised dietary exposure assessment. BEAD does not rely solely upon USDA for surveys of agricultural chemical use. At the same time, estimates of maximum percent crop treated are based on year-to-year variability. For the case of corn, this variability may have led to overestimates of maximum likely percent crop treated. Therefore, BEAD is amending its estimate for corn to an average of 75% of crop treated, with a likely maximum of 84% crop treated.

‘ Label changes: When listing a registrant’s proposed label change for a specific use on an atrazine label, the identity of the registrant should be disclosed.

HED Response:

Comment noted.

G. Ecotoxicology

‘ Aquatic Risk Assessment: The EPA preliminary environmental fate and effects document recognizes that refinements of the aquatic risk assessment (higher tiers) for atrazine are desirable and possible due to the wealth of toxicity, surface water monitoring, and modeling data for atrazine. Syngenta has sponsored an independent aquatic risk assessment that includes the highest level of refinement and uses additional atrazine specific data. We believe this independent panel assessment adequately addresses many of the concerns noted in the preliminary EPA document and this information will be submitted with our 30 day ecotoxicology response.

‘ Terrestrial Risk Assessment: Based on a preliminary assessment of the data used in the risk assessment, the small mammal/avian chronic toxicity values and terrestrial forage item residue values used in the preliminary risk assessment are incorrect. Additionally, use of appropriate toxicity values and realistic exposure scenarios will indicate minimal chronic risk to terrestrial species.

‘ Syngenta believes the there are fundamental process errors in the analysis of the incident reports and disagrees that these data suggest that atrazine poses a significant threat to ecological systems. For instance, the number of incidents reported (61 total) needs to be compared to the magnitude of atrazine use over the same time period to assess how the ecological incidents should be weighted. Also, it is inappropriate to assume in all incidents that atrazine was used alone. Syngenta is currently reviewing the internal incident data which are available to us, and also requesting the data that were used to generate the EPA analysis.

H. Mammalian Toxicology

‘ Toxicity Endpoint Selection: In the Preliminary Human Health Risk Assessment for Atrazine, EPA has incorrectly utilized NOELS defined in studies characterizing the effects of atrazine on the endocrine system of rodents in the development of assessments estimating risk for infants, neonates, juveniles, and adults. In the preliminary assessment, the NOEL from a 6 month chronic rodent study conducted in sexually mature female Sprague-Dawley rats was used to represent the intermediate-term exposure of infants, children, young adults, and adults. Syngenta recommends this preliminary determination be reconsidered because there are shorter duration studies targeting selected age brackets that better represent these population subgroups (See Table 1 for Toxicity Endpoints).

HED Response:

At a HIARC meeting subsequent to the release of the preliminary risk assessment [December 21, 2000], it was concluded that, although the endpoint selected for intermediate-term exposure of infants, children, young adults, and adults is derived from a 6-month study, it is reasonable to consider for an intermediate exposure duration, because data from a one month study showed effects on LH surge at 2.5 mg/kg/day after one month of dosing [from nonrepeat bleed measures]. Additionally, the intermediate exposure period is defined as 30 days to several months. With respect to the issue of relevance of endpoint to all age groups, see responses below.

‘ FQPA Uncertainty Factor: EPA’s preliminary decision to retain the FQPA 10x uncertainty factor is not supported by the data for all age groups and exposure durations as discussed below.

HED R ‘ esponse:

HED notes that this is not an error correction comment. The determination that the FQPA SF is appropriate for all age groups is supported by the nature of the effect of concern [neuroendocrine disruption], as well as evidence of neuroendocrine alteration after short-term exposure [PND 1-9], and uncertainties with respect to possible effects from exposure during development, which have not been thoroughly examined. As discussed in the preliminary risk assessment, neuroendocrine alterations of the hypothalamic-pituitary axis of rodents following Atrazine exposure are observed in chronic studies at low doses and in shorter-term studies at higher doses. Atrazine’s effect on ovarian cycling and the pre-ovulatory LH surge, as well as its effects on pregnancy, puberty, suckling-induced prolactin release, which leads to prostatitis, are viewed as neuroendocrinopathies or biomarkers indicative of Atrazine’s ability to alter hypothalamic-pituitary function in general. The mode of action for prostate inflammation and delayed puberty [effects on the young animal] is believed to be similar to the mode of action described for Atrazine-associated cancer [effects in the adult animal] and involves CNS neuroendocrine alterations.

Although Atrazine exposure is not associated with apparent cancer consequences in humans, a potential for noncancer effects due to its ability to disrupt hypothalamic-pituitary function cannot be discounted.

‘ Infant and Children Sensitivity: Developmental toxicity studies conducted on atrazine at NHEERL have been cited as evidence that infants are more sensitive than adults. In fact, the lowest atrazine NOEL (1.8 mg/kg/day) is derived from a chronic study where atrazine was administered to adult female Sprague-Dawley rats for 6 months. The NOELS for all developmental parameters evaluated (effects on in utero development [NOEL = 50 mg/kg/day][1], effect on prolactin secretion during the early post-partum period [NOEL = 13 mg/kg/day][2], effect on male preputial separation [NOEL = 6.3 mg/kg/day][3] and effect on vaginal opening [NOEL = 25 mg/kg/day][4] all were observed at higher doses indicating that developing organisms are less sensitive than adults.

HED Response:

HED notes that this is not an error correction comment. The registrant is correct in noting that the lowest atrazine NOAEL is derived from a chronic rat toxicity study. The other studies cited by the registrant reflect dosing for shorter periods of time. The registrant is also correct in noting that developmental toxicity studies conducted on atrazine at NHEERL are evidence that infants are more sensitive than adults. As noted in the FQPA SFC memo, quantitative increased susceptibility was demonstrated in a prenatal developmental toxicity study with DACT in rats: developmental effects were seen in the absence of maternal toxicity. The maternal NOAEL was 25 mg/kg/day, based on statistically significant decrease in body weight gain at 75 mg/kg/day (LOAEL). The developmental NOAEL was 2.5 mg/kg/day based on increase incidences of incompletely ossified parietals, interparietals and unossified hyoids at 25 mg/kg/day (LOAEL). See detailed comments under Syngenta comments on Toxicology Chapter FQPA Considerations

‘ *in utero* Carcinogenicity study: The results from an *in utero* carcinogenicity study on atrazine indicates that exposure of female Sprague-Dawley rats to atrazine and its dealkylated metabolites *in utero*, during lactation, and during sexual maturation does not cause an increase in sensitivity to atrazine.[5]

HED Response:

The study [MRID 44005301] referred to has never been considered acceptable. The study authors themselves considered this *in utero* carcinogenicity study to have too many short-comings in the conduct of this study to render the results interpretable for any parameter. Furthermore, appropriate endpoints to evaluate atrazine’s and DACT sensitivity/ susceptibility were not included in the study design.

Therefore this study is not reliable for drawing conclusions regarding potential risks to children.

- Developmental toxicity: In the developmental toxicity study conducted in rat on diaminochlorotriazine[6] EPA concluded that the fetal and maternal NOELs in this study were 2.5 and 25 mg/kg/day, respectively, whereas the study director at the performing laboratory concluded that the fetal and maternal NOELS were both 2.5 mg/kg/day. Based on this difference in interpretation, EPA has requested that Syngenta conduct a multigeneration reproduction study on diaminochlorotriazine. Sygnenta agrees that an additional developmental toxicity study is needed to better characterize the dose-response relationship because of the discrepancy in interpretation of this study by EPA and the performing laboratory.

HED Response:

The requirement for a multigeneration reproduction study is not to resolve the difference in interpretation of the DACT developmental toxicity study in rats; i.e., difference in maternal NOAEL set by study author and HED. That is not the issue. The issue is one of apparent increased sensitivity/susceptibility observed in the DACT developmental toxicity study. Agency toxicologists have concluded that quantitative increased susceptibility/sensitivity was demonstrated in a prenatal developmental toxicity study with DACT in rats: developmental effects were seen in the absence of maternal toxicity. The maternal NOAEL was 25 mg/kg/day based on statistically significant decrease in body weight gain at 75 mg/kg/day (LOAEL). The developmental NOAEL was 2.5 mg/kg/day based on increase incidences of incompletely ossified parietals, interparietals and unossified hyoids at 25 mg/kg/day (LOAEL). This conclusion was reached after thorough examination of the study, including historical control data and in light of the findings with respect to delayed puberty in both sexes and prostate inflammation following exposure of the maternal rat to Atrazine and the fact that the available data indicate that DACT exposure produces similar effects to those observed with Atrazine. The current guideline [OPPTS 870.3800] for the reproduction study provide for the measurement of parameters that assess the potential for neuroendocrine alterations. No new data or information have been provided to alter the Agency conclusions. An additional developmental toxicity study on DACT was not requested by the Agency.

- Request for a multigeneration reproduction study on diaminochlorotriazine: A multigeneration production study on diaminochlorotriazine(DACT) will not resolve the questions raised concerning *in utero* development (delayed ossification of bones) because these parameters are not evaluated in such studies. The multigeneration study conducted on atrazine[7] did not show any differences in the dose at which the adult and the fetus respond to treatment. If the EPA's conclusions about diaminochlorotriazine are correct, differences should have occurred because metabolism studies[8] have demonstrated that the major rodent

metabolite of atrazine is diaminochlorotriazine. Syngenta would appreciate an opportunity to further discuss with the Agency the rationale of the conduct of this study using DACT.

HED Response:

The requirement for conducting a multigeneration reproduction study is not to resolve "the questions raised concerning *in utero* development [delayed ossification of bones]", but to assess the potential of DACT to produce neuroendocrine alterations [see response above]. The Agency has requested a multigeneration reproduction study on DACT because the available data indicate that DACT exposure produces similar effects to those observed with Atrazine, and the current two-generation reproduction study protocol [OPPTS 870.3800 guideline] has parameters that are sensitive to endocrine disruption of reproductive development and function. It is also recommended that the F2 generation in this study be maintained for 120 days in order to evaluate the incidence of prostate inflammation. The Agency is also willing to engage in further discussion with the Registrant regarding the merit of the requirement for conducting this study.

- LH surge suppression studies: Syngenta has conducted two studies[9,10] to directly compare the effects of atrazine and diaminochlorotriazine on LH surge suppression in the female Sprague-Dawley rat; EPA has reviewed the first study[9] and the second study[10] is expected to be submitted to EPA in March, 2001. The results indicate that the NOELS for atrazine and diaminochlorotriazine are approximately the same.

HED Response:

HED will consider the registrant-sponsored LH data on DACT when available. It is to be noted that preliminary and unpublished studies from EPA's NHEERL (Dr. Cooper's laboratory) on delayed puberty in males also indicate that atrazine and DACT have similar NOAELs. Following review of the new study, HED will evaluate the need to reassess the NOAEL used in establishing the chronic RfD and the dermal and inhalation intermediate- and long-term occupational/residential exposure risk assessment scenarios for DACT.

- PBPK Studies: Syngenta is developing a physiologically based pharmacokinetic model (PBPK) to characterize and scale tissue dose in rodent studies to tissue dose in primates. The model will then be adjusted for developing organisms, and the magnitude of the scale factors will be determined. Using this method, Syngenta will determine the magnitude of the uncertainty factor needed when extrapolating from rodent to man.

HED Response:

HED must await the submission of the referenced models and an assessment of the data/information and will consider such studies when made available by the Registrant.

‘ Additional safety factors / CNS Function: Extra safety factors for children exposed to chemicals that affect the function of the rodent CNS is triggered when there is evidence that infants and children may be more sensitive than adults. As discussed above, all the evidence indicates that in fact developing organisms are less sensitive than are adults to atrazine.

HED Response:

HED disagrees with the registrant and considers weight of the evidence based on available data from special studies and from guideline developmental toxicity studies, which indicate increased sensitivity/susceptibility of the young. As discussed in the FQPA report on atrazine, atrazine's CNS mode of action raises a significant concern for children. Given the lack of data characterizing this CNS mode of action with appropriate measures/parameter on earlier developmental periods and for longer durations of exposure throughout development, HED views the need of an additional 10X safety factor to be protective of children's health.

‘ Acute NOEL: Syngenta notes that the toxicity endpoint selected by EPA for acute exposure is based upon a developmental effect (delayed bone ossification) and not endocrinological or central nervous system effects. EPA should drop the FQPA 10X factor for acute risk assessment.

HED Response:

HED disagrees with the Registrant that the FQPA 10X factor should be dropped for acute risk assessment. The toxicity endpoint selected for acute exposure [HIARC meeting (December 21, 2000) subsequent to the release of the preliminary risk assessment] is based on a weight of the evidence consideration, and the actual NOAEL and endpoint from which the reference dose is calculated is derived from one of the four studies [two developmental toxicity studies in rats, a developmental toxicity study in rabbits, and a study examining the effects of maternal Atrazine exposure during lactation on prostate effects in male offspring]. Any of the four studies may be appropriate for selection of an endpoint for acute risk assessment. The developmental effects observed in the two rat and one rabbit developmental toxicity studies [delayed or lack of ossification of several sites] are assumed to have the potential to occur after a single dosing. The effects observed in the open literature prostatitis paper [decreased suckling-induced prolactin release and increased incidence of prostatitis in male offspring] occur after only four days of dosing. The developmental NOAEL chosen is 10 mg/kg/day, based on delayed or lack of ossification of several sites at LOAEL of 70 mg/kg/day, and this is supported by the decreased suckling-induced prolactin release and increased

incidence of prostatitis observed at LOAEL of 25 mg/kg/day [NOAEL of 12.5 mg/kg/day]. To the extent that decreased prolactin levels can serve as a biomarker for effects on neuroendocrine control, there is a linkage between pubertal development and an effect on the hypothalamic-pituitary axis.

- Uncertainty over Magnitude of Exposure via Drinking Water: The preliminary risk assessment expresses some uncertainty about the magnitude of exposure of the population to total chlorotriazine when, in fact, Syngenta has conducted an extensive characterization of the concentration of atrazine and its metabolite concentrations in potable surface and groundwater (to be submitted). Furthermore, Syngenta has developed and submitted regression equations to predict total chlorotriazine concentrations in surface water based on monitoring data for atrazine and its chloro-triazine degradates. These data show that total chloro-triazine concentrations in surface water are no greater than a factor of two times the corresponding atrazine concentrations. Similar work is underway to characterize total chloro-triazine concentrations in groundwater CWS.

Deterministic vs. Probabilistic Risk Assessment for Drinking Water

EPA has acknowledged that the deterministic risk assessment on total chlorotriazine exposure via diet and water would likely be conservative. Syngenta has conducted a probabilistic risk assessment on the aggregate dietary (deterministic estimates from EPA's draft RED) and drinking water concentrations of total chlorotriazines (calculated using EPA regression equations) in surface water for 28 community water systems (Table 2) that reported some of the highest exposure values. The assessment was conducted on the combined monitoring data from Syngenta (PLEX and the Voluntary Monitoring Program) and the Acetochlor Registration Partnership (ARP). Toxicity endpoints were based upon the most sensitive endpoints for each exposure duration and subpopulation in Table 1.

Distributions of total chlorotriazine daily doses (Acute), monthly average daily doses (Short-Term), quarterly average daily doses (Intermediate-Term / two scenarios), and lifetime average daily doses (Chronic) were determined and expressed as a percentage of the acute, short-term, intermediate-term and chronic RfD for atrazine.

The results are summarized in Table 3 and the estimated daily doses and their respective percentiles are presented in Appendices 1-5 and 6-10, respectively.

The results indicate that none of the 28 community water systems exceeded the Drinking Water Level of Comparison for the Acute, short-term (Monthly Average), intermediate term (Quarterly Average), long term (Annual Average) or life time (Average calculated over a lifetime) at the 99.9^{th} percentile of exposure. Please note that although the extra 10X uncertainty factor was employed to calculate the RfD's used in the drinking water assessment, Syngenta does not believe that application of the factor for atrazine is scientifically valid.

HED Response:

HED intends to review the submitted probabilistic assessment, and will likely pursue a probabilistic assessment for a poriton of the CWS with resdiues of atrazine above levels of concern in the interest of further refining the risk estimates for those CWS.

Table 1. Summary of Toxicity Endpoints for Atrazine

Subpopulation/ Age	Toxicity Study NOEL (mg/kg/day)	UF* (100 + 10)	Adjusted RfD (mg/kg/day)	DWLOC* (ppb)
Acute Exposure (1 Day)				
Females 13 - 50	10 mg/kg/day	1000	0.01	298
Short Term Exposure (1-7 Days)				
Infants < 1 Year	13[a]	1000	0.013	90
Children 1-6 Years	6.3(50)[b]	1000	0.0063	81
Children 7-12 Years	6.3(50)[b]	1000	0.0063	186
Female 13-50	5[c]	1000	0.005	167
Male 13-19	5[c]	1000	0.005	189
Male 20+	5[c]	1000	0.005	189
All	5[c]	1000	0.005	189
Intermediate Term Exposure (7 Days – Several Months)				
Infants < 1 Year	13[a]	1000	0.013	90
Children 1-6 Years	6.3(50)[b]	1000	0.0063	81
Children 7-12 Years	6.3(50)[b]	1000	0.0063	186
Male or females 13-50	5[c]	1000	0.005	189
All	5[c]	1000	0.005	189
Long Term Exposure 3 Months – Lifetime				
All Subgroups	1.8[d]	1000	0.0018	68
All Subgroups	40[e,f]	1000	0.04	1511

* UF = 1000 proposed by EPA; the appropriate UF will be determined experimentally using PBPK models.

** DWLOC was calculated after the dietary contribution of atrazine was aggregated to exposure via water.

[a] Developmental NOEL = 13 mg/kg/day (Male Wistar Rat) Effect on prolactin/prostatitis (Stoker et. al., 1999)[2].

[b] Developmental NOEL = 6.3 mg/kg/day (Male Wistar Rat) Effect on preputial separation (Stoker et. al., 2000)[3] ; Developmental NOEL = 50 mg/kg/day (Male SD Rat) Effect on preputial separation (Trentacosta et.al. In press)[14]; DWLOC calculated from the 6.3 mg/kg/day NOEL.

[c] Subchronic NOEL = 5 mg/kg/day (Female SD Rat) LH surge suppression (Morseth, S. et.al., 1996a)[11].

[d] Chronic NOEL = 1.8 mg/kg/day (Female SD Rat) LH surge suppression (Morseth, S. et.al., 1996b)[12]

[e] Chronic NOEL = 40 mg/kg/day; (Female Fischer 344 Rat) Estrous cycle disruption (Thakur A.K, 1991) [13]

[f] Chronic NOEL = 40 mg/kg/day (Fischer-344 rats) LH surge suppression (Submission 3/2001).

Table 2. Location of 28 Selected Community Water Systems (CWSs)

CWS Index	Location				
	CWS #	CWS Name	City	County	State
1	IA5903011	Chariton Municipal Water Works	Chariton	Lucas	IA
2	IL0050300	Sorento Water Treatment Plant	Sorento	Bond	IL
3	IL0250100	Flora Water Treatment Plant	Flora	Clay	IL
4	IL0470200	W. Salem Water Treatment Plant	West Salem	Edwards	IL
5	IL0510150	Farnia Water Treatment Plant	Farnia	Fayette	IL
6	IL0610400	White Hall Water Treatment Plant	White Hall	Greene	IL
7	IL1170150	Carlinville Water Works	Carlinville	Macoupin	IL
8	IL1170400	Gillespie Water Treatment Plant	Gillespie	Macoupin	IL
9	IL1170500	Hettick Water Supply	Hettick	Macoupin	IL
10	IL1170950	Shipman Water Treatment Plant	Shipman	Macoupin	IL
11	IL1175150	Palmyra-Modesto Water Commission	N Palmyra Twp	Macoupin	IL
12	IL1175200	ADGPTV Water Commission	North Otter Twp	Macoupin	IL
13	IL1210300	Kinmundy Water Treatment Plant	Kinmundy	Marion	IL
14	IL1210450	Salem Water Treatment Plant	Salem	Marion	IL
15	IL1214220	Centralia Water Treatment Plant	Centralia	Marion	IL
16	IL1350300	Hillsboro Water Treatment Plant	Hillsboro	Montgomery	IL
17	IL1910450	Wayne City Water Plant	Wayne City	Wayne	IL
18	IL0250250	Louisville Water Treatment Plant	Louisville	Clay	IL
19	IN5219006	Holland Water Department	Holland	Dubois	IL
20	IN5240008	North Vernon Water Department	North Vernon	Jennings	IN
21	IN5269001	Batesville Water Utility	Batesville	Ripley	IN
22	IN5272001	Scottsburg Water Treatment Plant	Scottsburg	Scott	IN
23	LA1047002	Iberville Water District #3	White Castle	Iberville	LA
24	MO1010363	Higginsville Water Treatment Plant	Higginsville	Lafayette	MO
25	MO2010112	Bucklin Water Department		Linn	MO
26	M02010812	Vandalia Water Treatment Plant	Vandalia	Audrain	MO
27	OH0801511	Sardinia Water Treatment Plant	Sardinia	Brown	OH
28	OH4502314	Newark Water Works	Newark	Licking	OH

Table 3. Number of Community Water Systems with Distributions of Average Daily Total Chlorotriazine Doses that Exceeded the DWLOC at the 100th and the 99.9th Percentile

Appendix Number	Basis for Reference Dose	Number of 28 CWS's Exceeding the DWLOC at the 100th Percentile				
		Infants	**Children 1 to 6**	**Children 7 to 12**	**Adults 13 to 50**	**All**
7	Acute	Not Applicable	Not Applicable	Not Applicable	0	Not Applicable
8	Short Term	1	1	1	0	4
9	Intermediate Term	0	0	0	0	2
10	Intermediate Term	0	0	0	0	2
11	Chronic	Not Applicable	Not Applicable	Not Applicable	Not Applicable	0
		Number of Estimated Dose Distributions with Less Than 99.9% Below the RfD among the 28 PWSs				
		Infants	**Children 1 to 6**	**Children 7 to 12**	**Adults 13 to 50**	**All**
7	Acute	Not Applicable	Not Applicable	Not Applicable	0	Not Applicable
8	Short Term	0	0	0	0	0
9	Intermediate Term	0	0	0	0	0
10	Intermediate Term	0	0	0	0	0
11	Chronic	Not Applicable	Not Applicable	Not Applicable	Not Applicable	0

Appendix 1 Estimated Total Chlorotriazine Daily Doses (Acute) at the 99.9th Percentile

CWS Index	Acute Daily Dose (mg/kg/day) at the 99.9th Percentile for Females Ages 13 – 50
1.	6.40E-04
2.	5.20E-04
3.	8.80E-04
4.	7.50E-04
5.	9.10E-04
6.	8.30E-04
7.	9.40E-04
8.	1.90E-03
9.	2.00E-03
10.	1.80E-03
11.	1.10E-03
12.	9.60E-04
13.	7.50E-04
14.	3.00E-03
15.	1.20E-03
16.	1.10E-03
17.	1.40E-03
18.	1.00E-03
19.	8.70E-04
20.	1.10E-03
21.	8.00E-04
22.	8.90E-04
23.	1.40E-03
24.	1.00E-03
25.	7.30E-04
26.	1.20E-03
27.	2.20E-03
28.	9.20E-04

Appendix 2 Estimated Monthly Average (Short-Term) Daily Total Chlorotriazine Doses at the 99.9th Percentile

CWS Index	Monthly Average Daily Dose (mg/kg/day) at the 99.9th Percentile				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	2.40E-03	1.00E-03	8.60E-04	5.70E-04	6.90E-04
2.	2.20E-03	9.00E-04	8.20E-04	5.20E-04	6.80E-04
3.	3.20E-03	1.20E-03	1.10E-03	6.90E-04	1.10E-03
4.	3.30E-03	1.20E-03	1.00E-03	7.70E-04	1.10E-03
5.	3.10E-03	1.30E-03	1.20E-03	7.80E-04	1.00E-03
6.	3.50E-03	1.50E-03	1.20E-03	8.00E-04	1.30E-03
7.	2.80E-03	1.20E-03	1.10E-03	6.60E-04	9.70E-04
8.	8.20E-03	3.00E-03	2.40E-03	1.70E-03	2.20E-03
9.	7.20E-03	2.50E-03	2.40E-03	1.80E-03	2.50E-03
10.	7.10E-03	2.90E-03	2.70E-03	1.80E-03	2.40E-03
11.	4.30E-03	1.80E-03	1.50E-03	1.10E-03	1.40E-03
12.	3.50E-03	1.30E-03	1.00E-03	7.60E-04	1.10E-03
13.	2.70E-03	1.00E-03	9.00E-04	7.20E-04	9.20E-04
14.	1.20E-02	4.50E-03	4.20E-03	2.70E-03	3.40E-03
15.	4.80E-03	2.10E-03	1.80E-03	1.10E-03	1.60E-03
16.	5.60E-03	1.60E-03	1.50E-03	1.10E-03	1.40E-03
17.	4.20E-03	1.60E-03	1.10E-03	1.10E-03	1.10E-03
18.	3.90E-03	1.70E-03	1.60E-03	9.10E-04	1.30E-03
19.	3.70E-03	1.60E-03	1.30E-03	8.30E-04	1.10E-03
20.	3.70E-03	1.60E-03	1.30E-03	8.10E-04	1.00E-03
21.	3.20E-03	1.30E-03	1.10E-03	7.70E-04	9.00E-04
22.	4.00E-03	1.60E-03	1.40E-03	8.70E-04	1.50E-03
23.	4.20E-03	1.80E-03	1.40E-03	9.80E-04	1.40E-03
24.	4.30E-03	1.80E-03	1.60E-03	1.00E-03	1.60E-03
25.	2.70E-03	1.10E-03	1.10E-03	7.30E-04	9.70E-04
26.	4.80E-03	1.70E-03	1.50E-03	1.00E-03	1.50E-03
27.	9.30E-03	3.80E-03	3.00E-03	2.10E-03	2.60E-03
28.	2.10E-03	7.40E-04	6.20E-04	4.40E-04	6.20E-04

Appendix 3 Estimated Quarterly Average (Intermediate-Term) Daily Total Chlorotriazine Doses at the 99.9th Percentile

CWS Index	Intermediate-Term Dose = Quarterly Average Daily Dose (mg/kg-day) Quarters: Jan/Mar, Apr/Jun, Jul/Sep, Oct/Dec				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	2.10E-03	8.20E-04	6.60E-04	4.60E-04	5.00E-04
2.	1.80E-03	8.20E-04	7.00E-04	4.40E-04	7.20E-04
3.	2.10E-03	8.80E-04	8.50E-04	5.40E-04	8.10E-04
4.	2.60E-03	1.20E-03	9.00E-04	6.20E-04	8.20E-04
5.	2.80E-03	1.00E-03	9.60E-04	6.80E-04	8.90E-04
6.	3.30E-03	1.50E-03	1.20E-03	7.70E-04	1.30E-03
7.	2.10E-03	9.20E-04	7.80E-04	5.10E-04	7.90E-04
8.	5.80E-03	2.10E-03	1.80E-03	1.40E-03	1.60E-03
9.	5.10E-03	2.10E-03	1.80E-03	1.20E-03	1.80E-03
10.	6.90E-03	2.90E-03	2.80E-03	1.50E-03	2.80E-03
11.	4.10E-03	1.70E-03	1.60E-03	9.70E-04	1.50E-03
12.	2.30E-03	9.60E-04	8.70E-04	5.40E-04	9.90E-04
13.	2.30E-03	9.40E-04	8.50E-04	5.30E-04	8.50E-04
14.	7.10E-03	2.80E-03	2.30E-03	1.70E-03	2.20E-03
15.	3.10E-03	1.40E-03	1.20E-03	7.50E-04	1.10E-03
16.	3.10E-03	1.10E-03	1.00E-03	7.70E-04	9.00E-04
17.	2.20E-03	9.20E-04	8.10E-04	5.20E-04	8.10E-04
18.	3.00E-03	1.30E-03	1.20E-03	7.10E-04	1.00E-03
19.	3.60E-03	1.50E-03	1.20E-03	8.30E-04	1.00E-03
20.	2.10E-03	8.70E-04	8.10E-04	5.30E-04	7.30E-04
21.	3.30E-03	1.20E-03	1.00E-03	7.80E-04	9.00E-04
22.	3.90E-03	1.60E-03	1.30E-03	8.70E-04	1.10E-03
23.	2.00E-03	8.80E-04	8.10E-04	4.90E-04	8.60E-04
24.	3.20E-03	1.30E-03	1.20E-03	7.80E-04	1.20E-03
25.	2.90E-03	1.20E-03	1.00E-03	7.30E-04	8.90E-04
26.	2.80E-03	1.20E-03	9.70E-04	6.40E-04	1.10E-03
27.	6.30E-03	2.60E-03	2.40E-03	1.40E-03	1.90E-03
28.	1.30E-03	5.80E-04	5.60E-04	3.30E-04	0.00049

Appendix 4 Estimated Quarterly Average (Intermediate-Term) Daily Total Chlorotriazine Doses at the 99.9th Percentile

CWS Index	Intermediate-Term Dose = Quarterly Average Daily Dose (mg/kg-day) Quarters: Feb/Apr, May/Jul, Aug/Oct, Nov/Jan				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	2.00E-03	8.60E-04	7.40E-04	5.00E-04	6.00E-04
2.	1.80E-03	7.90E-04	7.30E-04	4.40E-04	6.60E-04
3.	2.10E-03	8.90E-04	8.00E-04	5.50E-04	7.60E-04
4.	2.20E-03	9.70E-04	8.70E-04	5.20E-04	8.40E-04
5.	2.50E-03	9.60E-04	8.90E-04	6.00E-04	9.50E-04
6.	3.30E-03	1.40E-03	1.20E-03	7.60E-04	1.30E-03
7.	2.30E-03	1.00E-03	9.10E-04	5.60E-04	8.60E-04
8.	6.00E-03	2.50E-03	2.00E-03	1.40E-03	1.60E-03
9.	6.20E-03	2.30E-03	2.10E-03	1.50E-03	2.00E-03
10.	6.80E-03	2.90E-03	2.70E-03	1.80E-03	2.30E-03
11.	4.30E-03	1.80E-03	1.60E-03	9.60E-04	1.50E-03
12.	2.60E-03	1.10E-03	9.40E-04	6.50E-04	1.00E-03
13.	2.50E-03	9.30E-04	8.30E-04	6.00E-04	8.10E-04
14.	7.20E-03	3.10E-03	2.70E-03	1.70E-03	2.40E-03
15.	2.90E-03	1.30E-03	1.20E-03	7.00E-04	1.20E-03
16.	3.00E-03	1.30E-03	1.10E-03	7.20E-04	9.90E-04
17.	2.60E-03	9.70E-04	8.70E-04	6.20E-04	7.50E-04
18.	3.20E-03	1.30E-03	1.20E-03	7.50E-04	1.00E-03
19.	2.90E-03	1.30E-03	1.20E-03	7.40E-04	9.50E-04
20.	2.70E-03	1.00E-03	8.50E-04	6.80E-04	8.20E-04
21.	2.90E-03	1.20E-03	9.80E-04	7.40E-04	8.20E-04
22.	3.10E-03	1.30E-03	1.20E-03	7.30E-04	1.10E-03
23.	2.80E-03	1.20E-03	1.10E-03	6.30E-04	9.70E-04
24.	4.30E-03	1.60E-03	1.40E-03	9.40E-04	1.20E-03
25.	2.70E-03	1.10E-03	1.10E-03	5.80E-04	1.10E-03
26.	2.70E-03	1.10E-03	1.00E-03	6.90E-04	1.10E-03
27.	7.50E-03	3.00E-03	2.80E-03	1.80E-03	2.30E-03
28.	1.20E-03	5.10E-04	4.80E-04	3.20E-04	5.30E-04

Appendix 5 Estimated Lifetime Average (Chronic) Daily Total Chlorotriazine Doses at the 99.9th Percentile

CWS Index	Chronic Dose = Lifetime Average Daily Dose at the 99.9th Percentile for the General Population
1.	1.70E-04
2.	1.90E-04
3.	1.80E-04
4.	2.80E-04
5.	3.20E-04
6.	2.30E-04
7.	2.80E-04
8.	2.70E-04
9.	5.70E-04
10.	4.50E-04
11.	3.70E-04
12.	3.40E-04
13.	1.60E-04
14.	3.40E-04
15.	2.90E-04
16.	2.60E-04
17.	1.90E-04
18.	2.50E-04
19.	1.80E-04
20.	1.50E-04
21.	2.40E-04
22.	1.80E-04
23.	2.20E-04
24.	2.40E-04
25.	1.30E-04
26.	2.80E-04
27.	1.90E-04
28.	1.00E-04

Appendix 6 Percentage of the Estimated Distribution of Daily (Acute) Doses Below the Acute RfD

CWS Index	Percentage Below Acute RfD for Females Age 13 – 50 Years
1.	100%
2.	100%
3.	100%
4.	100%
5.	100%
6.	100%
7.	100%
8.	100%
9.	100%
10.	100%
11.	100%
12.	100%
13.	100%
14.	100%
15.	100%
16.	100%
17.	100%
18.	100%
19.	100%
20.	100%
21.	100%
22.	100%
23.	100%
24.	100%
25.	100%
26.	100%
27.	100%
28.	100%

Appendix 7 Percentage of the Estimated Distribution of Monthly Average (Short-Term) Daily Total Chlorotriazine Doses Below the Short-Term RfD

CWS Index	Percentage Below Short-Term RfD				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	100%	100%	100%	100%	100%
2.	100%	100%	100%	100%	100%
3.	100%	100%	100%	100%	100%
4.	100%	100%	100%	100%	100%
5.	100%	100%	100%	100%	100%
6.	100%	100%	100%	100%	100%
7.	100%	100%	100%	100%	100%
8.	100%	100%	100%	100%	100%
9.	100%	100%	100%	100%	100%
10.	100%	100%	100%	100%	99.99%
11.	100%	100%	100%	100%	100%
12.	100%	100%	100%	100%	100%
13.	100%	100%	100%	100%	100%
14.	99.95%	99.98%	99.99%	100%	99.96%
15.	100%	100%	100%	100%	100%
16.	100%	100%	100%	100%	99.99%
17.	100%	100%	100%	100%	100%
18.	100%	100%	100%	100%	100%
19.	100%	100%	100%	100%	100%
20.	100%	100%	100%	100%	100%
21.	100%	100%	100%	100%	100%
22.	100%	100%	100%	100%	100%
23.	100%	100%	100%	100%	100%
24.	100%	100%	100%	100%	100%
25.	100%	100%	100%	100%	100%
26.	100%	100%	100%	100%	100%
27.	100%	100%	100%	100%	99.98%
28.	100%	100%	100%	100%	100%

Appendix 8 Percentage of the Estimated Distribution of Quarterly Average (Intermediate-Term) Daily Dose Below the Intermediate-Term RfD

CWS Index	Percentage Below Intermediate-Term RfD Quarters: Jan/Mar, Apr/Jun, Jul/Sep, Oct/Dec				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	100%	100%	100%	100%	100%
2.	100%	100%	100%	100%	100%
3.	100%	100%	100%	100%	100%
4.	100%	100%	100%	100%	100%
5.	100%	100%	100%	100%	100%
6.	100%	100%	100%	100%	100%
7.	100%	100%	100%	100%	100%
8.	100%	100%	100%	100%	100%
9.	100%	100%	100%	100%	100%
10.	100%	100%	100%	100%	99.98%
11.	100%	100%	100%	100%	100%
12.	100%	100%	100%	100%	100%
13.	100%	100%	100%	100%	100%
14.	100%	100%	100%	100%	99.99%
15.	100%	100%	100%	100%	100%
16.	100%	100%	100%	100%	100%
17.	100%	100%	100%	100%	100%
18.	100%	100%	100%	100%	100%
19.	100%	100%	100%	100%	100%
20.	100%	100%	100%	100%	100%
21.	100%	100%	100%	100%	100%
22.	100%	100%	100%	100%	100%
23.	100%	100%	100%	100%	100%
24.	100%	100%	100%	100%	100%
25.	100%	100%	100%	100%	100%
26.	100%	100%	100%	100%	100%
27.	100%	100%	100%	100%	100%
28.	100%	100%	100%	100%	100%

Appendix 9 Percentage of the Estimated Distribution of Quarterly Average (Intermediate-Term) Daily Dose Below the Intermediate-Term RfD

PWS Index	Percentage Below Intermediate-Term RfD Quarters: Feb/Apr, May/Jul, Aug/Oct, Nov/Jan				
	Infants	Children 1 to 6	Children 7 to 12	Adults 13 to 50	All
1	100%	100%	100%	100%	100%
2.	100%	100%	100%	100%	100%
3.	100%	100%	100%	100%	100%
4.	100%	100%	100%	100%	100%
5.	100%	100%	100%	100%	100%
6.	100%	100%	100%	100%	100%
7.	100%	100%	100%	100%	100%
8.	100%	100%	100%	100%	100%
9.	100%	100%	100%	100%	100%
10.	100%	100%	100%	100%	99.99%
11.	100%	100%	100%	100%	100%
12.	100%	100%	100%	100%	100%
13.	100%	100%	100%	100%	100%
14.	100%	100%	100%	100%	99.99%
15.	100%	100%	100%	100%	100%
16.	100%	100%	100%	100%	100%
17.	100%	100%	100%	100%	100%
18.	100%	100%	100%	100%	100%
19.	100%	100%	100%	100%	100%
20.	100%	100%	100%	100%	100%
21.	100%	100%	100%	100%	100%
22.	100%	100%	100%	100%	100%
23.	100%	100%	100%	100%	100%
24.	100%	100%	100%	100%	100%
25.	100%	100%	100%	100%	100%
26.	100%	100%	100%	100%	100%
27.	100%	100%	100%	100%	100%
28.	100%	100%	100%	100%	100%

Appendix 10 Percentage of the Estimated Distribution of Lifetime Average Daily Doses (Chronic) Below the Chronic RfD

CWS Index	Percentage Below Chronic RfD (0.0018 mg/kg-day)
1	100%
2.	100%
3.	100%
4.	100%
5.	100%
6.	100%
7.	100%
8.	100%
9.	100%
10.	100%
11.	100%
12.	100%
13.	100%
14.	100%
15.	100%
16.	100%
17.	100%
18.	100%
19.	100%
20.	100%
21.	100%
22.	100%
23.	100%
24.	100%
25.	100%
26.	100%
27.	100%
28.	100%

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Attachment 1

Syngenta's Comments on EPA's November 15, 2000 "Atrazine: Toxicology Chapter of the Reregistration Eligibility Decision"

Corrections for:

Atrazine: Toxicology Chapter of the Reregistration Eligibility Decision.

1. Section 4.9 Special/Other Studies, 4.9.1, pages 22 through 27; 4.9.2, pages 28 and 29. There are numerous instances of incomplete units of measurement or special symbols not included in the text.

HED Response:

The appropriate units of measurement have been inserted into the document, and the "short-hand" abbreviations/symbols have been identified; e.g., LDT, MDT, and HDT refer to the lowest, middle, and highest dose tested; SS should read either statistically significant or statistically-significantly.

2. Section 4.10 Toxicology data for major metabolites of atrazine, 4.10.1 Diaminochlorotriazine metabolite (DACT) –2-chloro-4-amino-6-amino s-triazine: didealkyl atrazine; G-28273; 870.3100 – Subchronic oral toxicity in rats.

DACT was fed to Sprague-Dawley rats for 90-days at concentrations of 0,10, 100, 250 or 500 ppm (MRID 43013207). Effects on body weight gain were observed at 250 and 500 ppm in females and males at 500 ppm. No other effects were observed in males at 10, 100 and 250 ppm. In addition, the authors of this study concluded that estrous cycle length and increase in the incidence of females exhibiting cycles with prolonged or persistent estrus and/or diestrus at 100 ppm and above. Since the completion of this study in 1991, however, Syngenta has commissioned another study in 1999 that was conducted at Covance Laboratories [Covance Study 6117-399 (Atrazine/Simazine/DACT Bridge Study)]. This study has a 26-week treatment phase in which 16 female Sprague-Dawley rats/group were fed diet containing DACT at concentrations of 0, 17, 34, 48 and 270 ppm (Final Report - 3/01). The cyclicity of these females were evaluated at Weeks 1-2, 5-6, 9-10, 13-14, 17-18, 21-22, and 25-26. It is anticipated based on preliminary findings that the duration of the estrous cycle or the incidence of females exhibiting prolonged or persistent estrus and/or diestrus will be noted at 17, 34, or 48 ppm. The NOEL should be 48 ppm or approximately 5 mg/kg/day.

HED Response:

HED notes that these comments reflect differences in data intrepretation and are not "error correction" comments. With regard to the subchronic oral toxicity study in rats exposed to DACT [the diaminochloro-triazine metabolite] at dose levels of 0, 10, 100, 250, and 500 ppm, Syngenta refers to a study commissioned in 1999 that has a 26-week phase in which female Sprague-Dawley [SD] rats were orally administered DACT *via* the diet, and cyclicity of these females was evaluated at various time points. The final report will be available, apparently, in March, 2001.

Based on preliminary findings, it is stated that the NOAEL "should be 48 ppm or approximately 5 mg/kg/day", presumably the NOAEL for the subchronic rat study [MRID 43013207]. The NOAEL is currently considered 0.7 mg/kg/day [10 ppm], based on estrus cycle effects at the LOAEL of 100 ppm [7.6 mg/kg/day]. The dose levels used in the referenced 1999 26-week study are listed as 0, 17, 34, 48, and 270 ppm.

When these data are available for consideration, HED will evaluate the need to reassess the NOAEL used in establishing the chronic RfD and the dermal and inhalation intermediate- and long-term occupational/residential exposure risk assessment scenarios for DACT.

3. Section 4.10 Toxicology data for major metabolites of atrazine, 4.10.1 Diaminochlorotriazine metabolite (DACT) –2-chloro-4-amino-6-amino s-triazine: didealkyl atrazine; G-28273; 870.3700 - Developmental toxicity in rats.

In this developmental toxicity study (MRID 41392402), 26 pregnant female Sprague-Dawley rats/group were administered atrazine by gavaged at 0, 2.5, 25, 75 and 150 mg/kg/day. The EPA reviewer suggested that the maternal LOAEL is 75 mg/kg/day, based on decreased body weight gain during dosing and NOAEL level is 25 mg/kg/day. However, the study authors, more conservatively, concluded that the maternal LOAEL was 25 mg/kg/day, based on transient treatment related reduction in food consumption (-10% at GD 6-8), and body weight gain (-32% at GD 6-8). The authors set the NOAEL lower than the EPA at 2.5 mg/kg/day. Both the EPA and study authors agree that the developmental LOAEL is 25 mg/kg/day based on incomplete ossification of the parietals, interparietals, and hyoids. Syngenta agrees with the study authors that the maternal and developmental NOAELs in this study are 2.5 mg/kg/day or higher considering the 10-fold difference between the NOAEL of 2.5 mg/kg/day and LOAEL of 25 mg/kg/day. More importantly, this developmental toxicity study with DACT does not shown any differential toxicity between the fetus and dams. This interpretation is consistent with the conclusions that the EPA has made in regard to atrazine and its mono-dealkylated metabolites. "There was no evidence of qualitative or quantitative increased susceptibility in two rat and one rabbit developmental toxicity studies using atrazine or in a rat developmental toxicity study using deisopropyl atrazine or a rat developmental toxicity using deethyl atrazine. There was no evidence of increased qualitative or quantitative susceptibility in the two-generation study using atrazine." [Excerpted from 6.0 FQPA CONSIDERATIONS; 6.1 Special Sensitivity to Infants and Children, page 62, paragraph 1].

HED Response:

With regard to the developmental toxicity study in rats exposed to DACT, Syngenta considers the NOAEL for maternal toxicity to be 2.5 mg/kg/day and not 25 mg/kg/day as determined by HED. The lower NOAEL is based on the transient treatment-related reduction in food consumption [-10% at GD 6-8] and body-weight gain [-32% at GD 6-8]. Also, the lower value is the NOAEL observed for developmental toxicity in the rat study. Currently, evidence of an increased sensitivity or susceptibility to infants and children from DACT exposure is based on this study. With respect to the issue of sensitivity/susceptibility, Syngenta reiterates the fact that there was no evidence of qualitative or quantitative sensitivity/susceptibility in two rat and one rabbit developmental toxicity studies or in the 2-generation reproduction study on Atrazine or in the rat developmental toxicity study on deisopropyl atrazine or deethyl atrazine.

Although the Agency concluded that an increased qualitative/ or quantitative a sensitivity/susceptibility was not observed in the guideline developmental or two-generation reproduction studies on Atrazine, it considers the findings from special rat studies designed to evaluate endocrine disruptors of prostate inflammation in male offspring and delayed puberty in both sexes treated with Atrazine and in u males with DACT to be evidence of increased susceptibility. These findings are and consistent with the Atrazine CNS mode of action. Furthermore, recent unpublished findings from EPA's National Health and Environmental Laboratory (i.e., Dr. Ralph Cooper) have shown that DACT also causes delayed puberty in male rats at similar concentrations of atrazine; thus suggesting that DACT has a similar CNS mode of action. The endpoints evaluated in these special studies se endpoints were not assessed in the guideline studies that have been conducted on Atrazine and DACT. It should be noted that the findings in the old (i.e., pre-1998) two- generation protocol in rats may be misleading because these pre-1998 guidelines did not include sensitive measures of endocrine disruption that are now included (e.g., estrous cyclicity, sperm measures, sexual maturation, expanded postmortem observations).

Finally, no new data/information have been submitted to justify a re-review of the issue of sensitivity/susceptibility of atrazine and DACT at this time.

4. 6.0 FQPA CONSIDERATIONS; 6.1 Special Sensitivity to Infants and Children, page 62.

Syngenta would re-iterate that there is no evidence of qualitative or quantitative increased susceptibility in two rat and one rabbit developmental toxicity studies using atrazine, a rat developmental toxicity study using deisopropyl atrazine, a rat developmental toxicity using deethyl atrazine, or the developmental toxicity study using 2-chloro-4-amino-6-amino s-triazine, DACT.
Additionally, the studies conducted on atrazine at NHEERL do not provide evidence that infants are more sensitive than adults. In fact, the lowest atrazine

NOEL (1.8 mg/kg/day) is derived from a chronic study where atrazine was administered to adult female Sprague-Dawley rats for 6 months. The NOEL was based on effects on the estrous, LH and prolactin surges at 3.65 mg/kg/day. The NOELS for all developmental parameters evaluated (effects on *in utero* development [NOEL = 50 mg/kg/day][1], effect on prolactin secretion during the early postpartum period [NOEL = 13 mg/kg/day][2] , effect on male preputial separation [NOEL = 6.3 mg/kg/day][3] and effect on vaginal opening [NOEL = 25 mg/kg/day][4]. NOEL values in these four studies were established at higher doses than in the chronic study conducted with adults indicating that developing organisms are less sensitive than adults are.

HED Response:

Regarding special sensitivity/susceptibility to infants and children, Syngenta reiterates their opinion that there is no evidence that infants are more sensitive than adults based on the lower NOAELs observed in studies on adult animals compared to studies on young animals. In the studies cited for "all developmental parameters evaluated", the NOAELs of 50 mg/kg/day [*in utero* development; exposure gestation days 1-8], 13 mg/kg/day [effect on prolactin secretion during early postpartum period; exposure days PND 23-53], 6.3 mg/kg/day [effects on male preputial separation; exposure days PND 1-4], and 25 mg/kg/day [effect on vaginal opening; exposure days PND 22-41] are compared to the lowest NOAEL observed for Atrazine [1.8 mg/kg/day], which was determined in the chronic oral toxicity study [6 months] in adult rats.

It should be noted that, irrespective of the chemical being dosed, dose levels causing effects in general are lower following the longer durations of exposure compared to short-term exposure; i.e., a higher dose is usually required to elicit an effect over a short exposure period compared to a long exposure period. In the special studies available in which the young animal was exposed to Atrazine, the durations of exposure were **4 days** for suppression of prolactin in dams and prostatitis effects on male offspring (PND 1-4; NOAEL 13 mg/kg/day),**10 days** [developmental toxicity; exposure days GD 6-15; delayed ossification; NOAEL 25 mg/kg/day]; **20 days** for delayed vaginal opening (PND 22-41; NOAEL 25 mg/kg/day), and **30 days** for delayed preputial separation (PND 23-53; NOAEL 6 mg/kg/day). In the two-generation reproduction study in rats, which is a longer-term exposure study, the NOAEL was 3.7 mg/kg/day [decreased body weight in males at PND 21 in both generations]. In the 6-month [chronic] study in the adult animal [NOAEL of 1.8 mg/kg/day], the effect/endpoint of concern was observed after 3 to 6 months of exposure. It is to be noted that in the 28-day study in 8-week old SD rats, the NOAEL was 5 mg/kg/day, based on estrous cycle alterations and attenuation of the LH surge at the LOAEL [40 mg/kg/day].

As discussed in the preliminary risk assessment, neuroendocrine alterations of the hypothalamic-pituitary axis of rodents following Atrazine exposure are observed in

chronic studies at low doses and in shorter-term studies at higher doses. Atrazine's effect on ovarian cycling and the pre-ovulatory LH surge, as well as its effects on pregnancy, puberty, suckling-induced prolactin release, which leads to prostatitis, are viewed as neuroendocrinopathies or biomarkers indicative of Atrazine's ability to alter hypothalamic-pituitary function in both young and adult animals in general. The mode of action for prostate inflammation and delayed puberty [effects on the young animal] is believed to be similar to the mode of action described for Atrazine-associated cancer [effects in the adult animal] and involves CNS neuroendocrine alterations. Although Atrazine exposure is not associated with apparent cancer consequences in humans, a potential for noncancer effects due to its ability to disrupt hypothalamic-pituitary function via a CNS mode of action cannot be discounted in the young for both short and longer durations of exposure.

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Attachment 2

Syngenta's Comments on Use/Usage and Labeling Noted in the EPA's November 30, 2000 Draft "Atrazine: HED's Preliminary Human Health Risk Assessment (and Associated EPA Documents) for the Reregistration Eligibility Decision (RED)

Summary

This section contains comments on usage and labeling information provided as background in the identified subject documents. Details are presented below.

Preliminary Human Health Risk Assessment

Detailed Comments:

1. Page 5, 6th Bullet Point; and Page 6: "Further reduction of the application rates for corn and sorghum to 2.5 lbs. a.i./acre/ year" should be qualified to note that this is a total of pre-emergence and post-emergence applications.

HED Response:

Corrected as per comment.

2. Page 6, 4th Paragraph, Line 2: Regarding the description of registered uses for atrazine ("Currently registered uses of atrazine"), please note that wheat as a registered use site is limited to Ecofallow programs where there is a sequence of fallow/crops grown following the atrazine treatment. In all ecofallow scenarios, treatment is to follow wheat harvest. Wheat is not a target crop. Also please qualify the use on "turf" as being limited to southern turfgrass, consistent with the species of turfgrass registered for atrazine.

HED Response:

Corrected as per comment.

3. Page 6, 4th Paragraph, Line 3: The characterization of the use of atrazine in CRP rangeland and the grazing prohibitions should be further clarified. The labeled use is limited to four states, OK, NE, OR, and TX. Grazing or cutting and feeding of hay on CRP acres are not permitted, except for severe drought conditions. But, if atrazine was used, grazing and making of hay are restricted. Only beef cattle are placed in these CRP situations. If atrazine is used in CRP establishment, it is usually during the first year of the program, and there is insufficient grass growth during a drought season for grazing or making of hay to be practical. Therefore, it is not appropriate to factor rangeland use into the dietary intake for dairy cattle.

HED Response:

HED has further characterized the CRP rangeland uses as per comment. HED notes that rangeland grasses were not included in the theoretical diets of cattle.

4. Page 7, 1st Paragraph, Line 2: "Atrazine is formulated variously as dry flowables, emulsifiable concentrates, and ready-to-use solutions." Please note that to our knowledge, formulation technology for atrazine does not allow for emulsifiable concentrates. Only water-based flowable formulations are currently registered. Also, there are no ready-to-use solutions of atrazine.

HED Response:

Corrected as per comment.

5. Page 14, 1st Paragraph, Line 6: In the "Preliminary risk estimates associated with occupational exposures to atrazine", relative to conifer use, further explanation of the use pattern is necessary. The exposure scenarios described in the document for aerial applications of atrazine in conifer forest situations are not realistic, due to a number of factors, including an incorrect assumption of a maximum of 1200 acres treated per day. This is a limited use pattern for atrazine, particularly in conifer forests and Christmas tree farms. Because of the nature of the terrain in these farms, helicopters must be used to make aerial applications. Due to limits in load capacity, small acreage sites, and limited hours of favorable weather conditions, helicopters can only spray a maximum of 150-350 acres/day, not the 1200 acres listed in the assessment. Furthermore, with relatively minor use of atrazine, applications would take place only over the course of a week, entailing only a short-term (and not intermediate-term) exposure. Only short-term risks should be calculated in association with this use pattern.

HED Response:

The daily acreage treated for conifer forests has been revised to a reasonable high daily limit of 350 acres, and the risk assessment has been changed to reflect this number. The Syngenta information is welcomed, and confirmed by a range of 67-343 acres as "typical to high" from surveys by NAAA (data supplied electronically by the NAAA on January 2-4, 2000). The Agency is seeking further information from all sources, including the USDA Forest Service.

6. Page 14, 1st Paragraph, Line 7 and Page 19, 1st Paragraph, Line 11: First paragraph and Page 19, Data Gaps; "The treatment, mixing, loading, and application of dry and liquid fertilizers, both commercially (including cooperatives) and on-farm…" Dry fertilizer impregnation of atrazine is **not possible** on farm, and must be conducted in a facility where proper equipment is present. On page 19 under Data Gaps, please note that on-farm impregnation of dry fertilizers is not possible, so such data should not be requested. Automated large-scale blenders, that use machinery that limits exposures, are used to prepare these fertilizer/atrazine preparations. In addition, the assumption that 960 tons of fertilizer is mixed and loaded within a day is not correct. The actual amount is more likely to be 150 - 300 tons. Syngenta will be submitting a document that will

more fully describe the treatment process, possible exposure scenarios, and risk calculations.

HED Response:

The Agency encourages submission of additional information to clarify this exposure scenario. The Agency believes, at a minimum, individual farmers may apply treated fertilizer, and encourages submission of information about daily acres fertilized and equipment used.

7. Page 36, 1st Paragraph, Line 4: "Section 4.0 Exposure Assessment, Summary of Registered Uses" indicates Novartis (now Syngenta) has orchard grass and hay uses labeled. This is incorrect as noted by EPA on page 6. Syngenta had requested these tolerances be withdrawn at the time the labeled use was deleted during the data call-in process. Also, the use on wheat and turf needs to be clarified as noted in comments above (i.e. for page 6).

HED Response:

Corrected as per comment. Tolerances for orchard grass and hay have been recommended for revocation under tolerance reassessment during the RED process.

8. Page 37, Table 4: Table 4 lists several Syngenta formulations as being registered, when two of these have been voluntarily cancelled (note: Bicep II and Bicep Lite II). Please remove these formulations from the registered formulations list. Also, the use on CRP rangeland should be clarified as noted in comments above. We also note the mention in the document of a product, Oxon Italia 5L, for use on roadsides; please note that this product registration is held by another registrant and that this product has uses not supported by Syngenta. The use rate for this formulation is equivalent to 2.5 lbs. a.i./A, which is higher than any other products labeled for the roadside use, including products registered by Syngenta. This rate is not supported by our data.

HED Response:

HED has verified that Bicep II and Bicep Lite II have been cancelled, and the appropriate changes have been made to the risk assessment documents. Products registered to other registrants must necessarily be considered in the reregistration process.

9. Page 46, 1st Paragraph, Line 6: "BEAD has recently updated the percent of crop treated (PCT) information for atrazine…..for other corn; 82%-97%." Novartis strongly disagrees with this PCT value, based on currently available market information. The USDA NASS reports for 1997, 1998, and 1999 show 69 to 70%

of the field corn acres receives an atrazine treatment. Furthermore, the 82% - 97% estimates cited are not possible, because rotational crop restrictions will prevent use on many acres in the north central part of IA and southern MN.

HED Response:

BEAD has revised the usage estimates on corn and the revised estimates have been incorporated into a revised dietary exposure assessment. BEAD does not rely solely upon USDA for surveys of agricultural chemical use. At the same time, estimates of maximum percent crop treated are based on year-to-year variability. For the case of corn, this variability may have led to overestimates of maximum likely percent crop treated. Therefore, BEAD is amending its estimate for corn to an average of 75% of crop treated, with a likely maximum of 84% crop treated.

10. Page 49, 4th Paragraph, Line 5: "Risk characterization and sources of uncertainties" includes in the fourth paragraph a discussion of illegal residues in leafy vegetables and wheat. Explanation of these is difficult since these crops are not registered and are very susceptible to injury caused by atrazine.

HED Response:

HED acknowledges and shares the registrant's concern that explaining these illegal residues in leafy vegetables and wheat is difficult; however, as these residues of atrazine have been detected under the USDA Pesticide Data Program (PDP) and FDA monitoring programs designed to detect illegal residues, the detections cannot be dismissed.

11. Page 50, 2nd Paragraph, Line 9: "Atrazine's moderate persistence in soils and high volume of usage are believed to create a reservoir of chemical available for movement down through the soil with irrigation and rainfall." This statement is not supported by either widespread groundwater monitoring data nor the environmental fate characteristics of atrazine as demonstrated in extensive laboratory persistence and mobility data and field dissipation data on parent atrazine and chloro and hydroxy metabolites.

HED Response:

HED has removed the statement as per the comment.

12. Page 73: In the paragraph starting "Even with coveralls, gloves, respirators,…..", there are several assumptions of use which are incorrect or overstated. For example, the assessments used to support this statement included the 4 lb. a.i./A roadside rate. To our knowledge, the only rate supported by actual residue data for this use is the 1 lb. a.i./A rate on our AAtrex labeling. Also, chemical fallow rates should not exceed 3 lbs. a.i./A and CRP rangeland use rates should not

exceed 2 lbs. a.i./A, since these are the limits supported by the available databases. Similarly, "largest quantities" of chemical handled is not appropriate for minor use of atrazine in forestry, fallow and CRP. Again, if other registrants have higher application rates than those mentioned above, they are not supported by adequate data and should not be used in the assessment.

HED Response:

The labels for this use do not clearly limit application to "roadsides" but instead "highway rights-of-way." There is no application equipment specified on the labels, so HED has used the closest equipment for which surrogate exposure data are available, which is commonly called the "right-of-way sprayer." There is little data on the equipment used or exposure information, so this is a best-estimate based on HED and BEAD experience. The labeled rates include, 1, 2, 2.2, and 4 lbs ai/acre and all are special local need (SLN) registrations. The 4 lbs ai/acre labels are still active but are dated 1985 and 1989. The Chemical Review Manager for atrazine is currently attempting to determine the need for continued registration of these SLN registrations, particularly at the higher application rates.

Product and Residue Chemistry Chapters

1. Page 3, 1st Paragraph, Line 3: In the "Description of Chemical", add "fallow programs" behind "wheat". Wheat per se is not a target crop for atrazine use. Same comment for Page 33. Also, not all crops can be treated using aerial application. The labels note aerial treatment is possible only when broadcast applications are specified.

HED Response:

Corrected as per comment.

2. Page 34, Table 1: Syngenta has requested voluntary cancellation of Bicep II and Bicep Lite II. These formulations should be removed from the assessment.

HED Response:

Correction has been made to the document as per comment.

3. Page 40, 5th Paragraph, Line 2: Under the section headed by "Magnitude of the Residue in Crop Plants", the sentence reads "The adequacy of submitted field trials for sugarcane and wheat is dependent on additional supporting data on storage stability". Please note that Syngenta is only supporting use on wheat as an ecofallow treatment post-harvest to wheat stubble. We do not support wheat as a target crop per se. This same comment applies to the discussion on page 42 under "Wheat".

HED Response:

This comment is duly noted, however, storage stability studies relate only to the reliability of analytical data that Syngenta has submitted. The storage stability data are meant to support existing field trial study data on these crops, and is an integral and standard part of any field trial study design. HED has acknowledged that wheat is not a target crop in the risk assessment.

4. Page 43, 6th Paragraph, Line 6: In the section headed by "Magnitude of the Residue in Processed Food/Feed", the EPA review describes the need for processing data in sugarcane at 5X the application rate per crop season. However, there would be concern to conduct such a study because of potential phytotoxicity to the sugarcane and application of these excessive rates on field sites with shallow water tables. Further, Syngenta must challenge the reasoning for such a request in the first place. The more recent processing study conducted at 2X the maximum label rate, did not indicate concentration of residues in processed commodities occurred. Same comment for page 57 under Tolerances Needed Under 40 CFR section 180.220(a)(1) for wheat hay.

HED Response:

HED agrees that it is unproductive to treat sugarcane at concentrations that would result in phytotoxicity and is dropping the requirement for a study at 5X the seasonal application rate. HED does recommend another processing study using crops incurred with as large residues as possible from application of as much atrazine is safe, as late in the season as reasonable. If residue concentration is not seen, such a processing study might also demonstrate a significant decrease in residues in sugar cane sugar that would allow increased refinement in future atrazine exposure assessments.

HED has reevaluated the need for geographically representative studies in wheat hay in response to this comment. Residues of atrazine in wheat forage, the wheat commodity with the highest residues, were up to 1.11 ppm, yielding a tolerance of 1.5 ppm in wheat forage. HED believes that a tolerance in wheat hay can be supported using the residues in wheat forage corrected for percent dry matter. Correcting 1.11 ppm for the ratio of percent dry matter between wheat forage and wheat hay (Hay/Forage = 88%/25% = 3.5), yields estimated residues in wheat hay at 3.9 ppm. From this HED proposes a tolerance in wheat hay at 5 ppm. If the registrant disagrees with this proposed tolerance, geographically representative studies must be submitted to support a different tolerance.

5. Page 57, 4th Paragraph, Line 7: In the section headed by "Tolerances to be Established Under 40 CFR section 180.220(a)(2), please note the following comments on Syngenta supported uses. Syngenta is not supporting perennial rye grasses or orchard grass as use patterns and we are not aware of any other

registrants supporting these uses. They should be deleted as tolerance requirements. Also, since wheat is not supported as a target crop, the need for tolerances in wheat straw and stover is questioned.

HED Response:

HED is recommending for the revocation of the tolerance for orchard grass and hay. HED is currently determining the status of the perennial rye grass tolerances. If there are no other parties (IR-4) with an interest in supporting the perrenial rye grass tolerance, this tolerance can also be recommended for revocation under tolerance reassessment during the RED process. Regarding tolerances for wheat straw and stover, there is an existing tolerance on wheat, which necessitates tolerances on food/feed items processed from wheat. If the registrant no longer wishes to support a tolerance on wheat, then they can petition to revoke the tolerance. However, this would make any atrazine residues incurred in wheat as a result of the application of atrazine products to wheat stubble in a wheat-corn-fallow rotation illegal. As noted, USDA monitoring has detected residues of atrazine in wheat.

6. Page 64, Table A: In Table A, under Broadcast for corn (Wheat-Corn-Fallow) in six states, the use rates specified are incorrect. The ND and SD maximum use at >7.5 pH is actually 1.5 lbs. a.i./A, not 1.4 as listed in the table; at <7.5 pH the maximum rate is actual 2 lbs. a.i./A, not 1.8 as listed in the table. Also on page 64, the table incorrectly lists 8 treatments per season to guava; the label indicates “do not apply more frequently than at 4-month intervals,” so there can only be 3 treatments per year.

HED Response:

Corrected as per comment.

7. Page 66, Table A: Wheat is noted as a target crop. Syngenta is only supporting wheat in various chemical fallow programs where atrazine is applied after wheat harvest. The use pattern allows treatment to wheat stubble after harvest and there is at least a 12 month interval from such a treatment to wheat planting. Note also that typical use practices would have growers using various tillage systems during this program. Application of atrazine at up to 1 lb. a.i./A will not provide weed control in wheat planted after the fallow period. Atrazine treatment after initial application to wheat stubble is not allowed in the chemical fallow program..

HED Response:

Corrected as per comment.

Occupational and Residential Exposure Assessment

1. Page 1, 1st Paragraph, Line 5: "It is used as a nonselective herbicide on several other crops, and is widely used on sod and turf, including home lawns and golf courses." Note that atrazine is not used as a nonselective herbicide on crops. Further, the use on sod and turf should be described properly; southern turfgrass is the appropriate designation.

HED Response:

Corrected as per comment.

2. Page 4, 2nd Paragraph, Line 5: It is incorrect to list certain of these uses as high rates. For instance, chemical fallow rates should not exceed 3 lbs. a.i./A and CRP rangeland use rates should not exceed 2 lbs. a.i./A, so it is not appropriate to characterize these uses as a high atrazine rates, nor "largest quantities" on minor use crops like forestry, chemical fallow programs and CRP land. Additionally, grasslands is not an accurate description of the use pattern for CRP rangeland, for reasons noted in other comments cited previously. If other registrants have higher rates, again, they are not supported by adequate residue data and therefore, should not be used in the assessment.

HED Response:

Corrected as per comment.

3. Page 4, 4th Paragraph, Line 3: Under the heading "Post-application Worker Exposure and Risk Estimates", the sentence reads "The lowest MOEs for trimming /harvesting Christmas trees (120) and harvesting sod (100), used transfer…exposure estimates". Please note that atrazine treatment is seldom or never followed by trimming/harvesting of trees, since atrazine is applied in spring and trees are harvested in the winter. Also, sod removal or harvesting has a 30 day restriction from application.

HED Response:

The Agency consulted with its experts including the Biological and Economic Analysis Division (BEAD) and agrees in principle with Syngenta's statement. Because all of the reentry exposures are not fully understood, and additional information is being sought, all of the postapplication worker exposure calculations for conifers and Christmas trees will be included for characterization purposes. Note that all risk estimates for the postapplication workers do not exceed HED's level of concern (MOE s are greater than 100 on the first day after treatment).

4. Page 6, 4th Paragraph, Line 1: Under the heading "Recommendation/Data Requirements" 2nd paragraph, the mixing of atrazine and fertilizers on farm is not

done. Dry fertilizer impregnation of atrazine is **not possible** on farm, and must be conducted in a facility where proper equipment is present. The statement should be modified as indicated. On page 19 under Data Gaps, please note that on-farm impregnation of fertilizers is not possible, so such data should not be requested. Automated large-scale blenders that limit exposures do these preparations. Syngenta will be submitting a document that will more fully describe the treatment process, possible exposure scenarios, and risk calculations.

HED Response:

The Agency encourages submission of additional information to clarify this exposure scenario. The Agency believes, at a minimum, individual farmers may apply treated fertilizer, and encourages submission of information about daily acres fertilized and equipment used.

5. Page 12, 3rd Paragraph, Line 6: In the section headed by "Summary of Use Patterns and Formulations", please clarify use on lawns and turf as being limited to Southern turfgrass only. Also in the listing of weeds controlled by atrazine in the 4th paragraph, eight of the weeds listed are partially controlled and should be so indicated.

HED Response:

Corrected as per comment.

6. Page 12, 5th Paragraph, Line 1: At the bottom of the page under the heading "Formulation types and percent active ingredient", there is an error. These include listing a 90% liquid formulation when, to our knowledge, there is no such formulation registered.

HED Response:

Corrected as per comment.

7. Page 13, 4th Paragraph, Line 2: Under the heading "Application Rates and Timing and Frequency of Application", the sentence reads "With the exception of sugarcane, guava, and macadamia nuts, the registrant has proposed a maximum label rate for all uses of 2.0 lbs. a.i./acre per application. Therefore, although exceptions are listed below, only the 2.0 lb. a.i./acre rate was assessed for the remaining uses." Syngenta questions to which "registrant" is the Agency referring? We are not aware of any agreement to limit the application rates as noted. Certainly, there exists on registered atrazine labels from Syngenta and others, uses that allow greater than a 2.0 lb. a.i./acre rate, i.e., conifers, southern turfgrass, and chemical fallow uses, all allow greater than 2.0 lbs. per treatment. Also, in this section, bottom of the page under "Turfgrass (spray applications)", it notes "There

is also a label supporting up to 4 lbs. a.i./acre in FL, which the registrant states will not be supported." Syngenta is not that registrant, but it should be noted our label allows 4 lbs. a.i./acre in muck soils in FL. This rate is necessary for efficacy reasons on this highly organic soil type.

HED Response:

Statement has been corrected.

8. Page 14, 6th Paragraph, Line 1: Under the same heading as noted in previous comment, for Sugarcane, it implies that " (All) Treatments are applied over the sugarcane. " This is incorrect. Only two applications are allowed after cane emergence. The other two are before cane emergence and at emergence.

HED Response:

Statement has been removed.

9. Page 36: In the section headed by "Baseline" at the bottom of the page, it notes the use rate on bermudagrass rights-of-way is 4 lbs. a.i./A. Syngenta section 24(c) labels only allow 2 lbs. a.i./A. If there are other registrants who have higher rates, we are not aware of them. Also, "grasslands" is not the same as CRP rangeland, for reasons stated elsewhere in these comments.

HED Response:

These use rates are registered currently under Special Local Need (SLN) labels. HED is in the process of ascertaining if they are currently active. Refer to Comment # 11 included in the responses to Attachment # 5.

10. Page 42, 4th Paragraph, Line 16: Under the section headed by "Assumptions Used in Post-Application Exposure Calculations", please note that for macadamia nuts, the label specifies "Do not spray by air". The comment "… although aerial application is also possible" should be removed.

HED Response:

HED concurs that the label for macadamia nuts specifies "Do not apply by air", and the correction has been made. Aerial application to macadamia nuts is no longer in text or tables.

11. Page 45, 1st Paragraph, Line 1: In the first sentence at the top of the page "The lowest MOEs, for trimming/harvesting Christmas trees and harvesting sod……conservative exposure estimate" it should be noted we previously

commented on the timing of atrazine application relative to these tasks in this document.

HED Response:

The Agency consulted with its experts including the Biological and Economic Analysis Division (BEAD) and agrees in principle with Syngenta's statement. Because all of the reentry exposures are not fully understood, and additional information is being sought, all of the postapplication worker exposure calculations for conifers and Christmas trees will be included for characterization purposes. Note that all risk estimates for the postapplication workers do not exceed HED's level of concern (MOE s are greater than 100 on the first day after treatment).

12. Page 74, Table 5: Table 5 indicates a bermudagrass right-of-way rate of 4 lbs. a.i./A, but this is not consistent with Syngenta's 24(c) labels that list a maximum of 2 lbs. a.i./A.

HED Response:

Refer to Comment # 11 included in the responses to Attachment # 5.

Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine

1. Page 5, 1st Paragraph, Line 4: In the second sentence, "…one was conducted based on a post-emergent application at 3 lbs. a.i./A (1.2x the typical pre-emergent/post emergent 2.5 lbs. a.i./A)." The word "typical" should be revised to "maximum". The same comment applies to the next part of this sentence as well. Also, comparing a post-emergent treatment to a combination of pre and post-emergent treatments is not appropriate. The rate of 3 lbs. a.i./A post-emergence is actually 1.5 X the maximum post-emergent rate of 2.0 lbs. a.i./A". Also using this same approach, the value for the TRR of 0.0005 ppm was based on a 1x rate. What would it be if the rate were adjusted by 0.5 lb. as noted above?

HED Response:

In response to this comment, the word "typical" has been changed to "maximum." The TRR available from the application at 3 lbs ai/A is the best TRR data available to HED to describe the portion of the corn crop where some portion of treatment is postemergent. The maximal seasonal rate is 2.5 lbs ai/A in the scenarios the registrant has provided as typical when there is some postharvest treatment of corn. The value of 3.0 lbs ai/A is correctly 1.2 X 2.5 lbs ai/A. To compare the resulting residues to 2.0 ai/A would require that HED introduce the assumption that no part of the residues persist from the pre-emergent treatment. Also, to reduce the residues from this 2.5 annual application rate by the factor of 1/1.2 (or by 1/1.5 as is suggested) would require information that the concentration of atrazine residues is exactly linear with the concentration of atrazine applied to the crop. HED does not have this information.

2. Page 6, 2nd Paragraph, Line 1: "For field corn, BEAD reported that, on average, 82% of the crop was treated, and at a maximum, 97% of the crop was treated with atrazine. As stated earlier in our comments, USDA NASS data for 1997– 1999 shows ~70% of corn acres receives atrazine. This value provides a more accurate average annual value. This same comment applies to the next paragraph that discusses the point estimate for the acute assessment for field corn.

HED Response:

BEAD has revised the usage estimates on corn and the revised estimates have been incorporated into a revised dietary exposure assessment. BEAD does not rely solely upon USDA for surveys of agricultural chemical use. At the same time, estimates of maximum percent crop treated are based on year-to-year variability. For the case of corn, this variability may have led to overestimates of maximum likely percent crop treated. Therefore, BEAD is amending its estimate for corn to an average of 75% of crop treated, with a likely maximum of 84% crop treated.

3. Page 7, 1st Paragraph, Line 5: "From this information…..18 residues at 0.0005 ppm…". Assuming the rate adjustment noted above, would this value need to be recalculated?

HED Response:

The usage estimates on sweet corn have not been revised, so these RDFs have not been revised.

4. Page 10-11, Several Paragraphs: It should be noted that wheat is not listed as a target crop for any registered atrazine products to our knowledge. All data generated by Syngenta for this crop in the past have been for the chemical fallow treatment regimes on our AAtrex formulations. All of these different fallow situations involve application of atrazine to wheat stubble after wheat is harvested. Application only occurs during the first year of the program, followed by different sequences of rotations to corn, sorghum, and wheat. Therefore wheat is actually a rotational crop only. Page 10, 5th Paragraph, Line 1: BEAD estimates that less than 1% of wheat is treated with atrazine, but in cases where BEAD reports <1% CT HED uses a default value of 1% CT. The USDA NASS report for 1998 shows ~ 60 million acres of all wheat. Thus, the default value of 1% CT means 600,000 acres is assumed to receive atrazine. This is not likely, for an unlabeled crop.

HED Response:

There is a tolerance for atrazine on wheat, and residues of atrazine have been found on wheat. Therefore wheat is included in the dietary assessment. Whether the assumption is 1% crop treated on wheat, or is less than 1% crop treated, is moot because the number of samples that actually tested positive for atrazine exceeded 1% of the total number of wheat samples. The language in the dietary exposure memo has been revised to explain this more clearly.

5. Page 12, 1st Paragraph, Line 1: "Macadamia Nuts", What is the source of the estimate that 57% of the crop is treated with atrazine.

BEAD Response:

BEAD recently received information drawn from a survey of pesticide use among Hawaiin macadamia nut growers. As a result, BEAD now believes the % crop-treated figure for macadamia nuts is closer to 57%.

6. Page 14, 3rd Paragraph, Line 8: Where the AR (anticipated residues) for acute dietary assessment was discussed, the 97% corn crop treated issue applies. See comment above on per-cent of corn acres treated with atrazine. This needs to be recalculated based on more accurate crop treated use estimates of ~ 70%, if NASS values are used.

HED Response:

The anticipated residues in milk have been revised per the revised usage estimates in corn from BEAD.

7. Page 15, Table 4: In Table 4, the percent of crop treated for corn commodities is incorrect. Refer to comment above on per cent of crop treated.

HED Response:

The anticipated residues in meat have been revised per the revised usage estimates in corn from BEAD.

8. Page 16, 1st Paragraph, Line 3: In the first paragraph below Table 5, it states "The highest %CT is corn at a maximum of 97% CT. Again, refer to other comments on per cent of crop treated.

HED Response:

The anticipated residues in meat have been revised per the revised usage estimates in corn from BEAD.

9. Page 18, Table 6: In Table 6, again, note that the percent crop treated figures for corn (82-97%) need to be adjusted to around 70%. Also the assumption of 100% of the sugarcane crop being treated is not realistic. We will provide updated information on sugarcane use in early 2001.

HED Response:

The commodity summary tables have been revised per the revised usage information from BEAD.

10. Page 19, Table 7: In Table 7, again, the percent crop treated figures for corn need to be corrected.

HED Response:

The commodity summary tables have been revised per the revised usage information from BEAD.

11. Page 22, 1st Paragraph: First full paragraph on the page, it was noted that only wheat residue monitoring data was used in the dietary exposure analysis. See comment for page 10-11 above for further explanation of wheat use. An explanation of the wheat use and the potential explanation for wheat residues should be added.

HED Response:

A comment to this effect has been added to the dietary exposure memorandum.

12. Page 40, Attachment 5: We would suggest that the Agency reformat Attachment 5 (RDF Files) as it is hard to follow and confusing to the reader.

HED Response:

Per this comment Attachment 5 has been reformatted. If this revision is still unclear please make specific comments.

13. Page 44, 1st Paragraph, Line 3: In the paragraph headed by "Quantitative Usage Analysis", it is stated that "Atrazine is also used on pineapples,….for these crops". Syngenta dropped the use of atrazine on pineapples during the early stages of reregistration for business reasons, declined to provide additional residue data, and requested the tolerance be withdrawn for atrazine. Therefore, it is not appropriate to cite it as a registered crop.

HED Response:

The attached Quantitative Usage Analysis has been revised and pineapples have been removed.

14. Page 45, Untitled Table: The table does not clarify where the values came from that were used. Was it a particular growing season, or simply an average of several years? If it was an average, please state which years are being averaged. Again, as noted several times, the per cent of crop treated for corn is too high (82-97%) and needs to be corrected to reflect available market surveys. Also, Syngenta is uncertain where the estimates of use on wheat acres were obtained. As noted in several of our comments, wheat is not a target crop, but a rotational crop in chemical fallow situations.

HED Response:

This is an attached Quantitative Usage Analysis. The Usage on corn has been revised. A header has also been added to this table.

15. Page 46, Untitled Table: In the same table as noted for page 45 above, the site "Woodlands" is noted. This is not a registered use for Syngenta, and is not supported by us through data support for re-registration, so unless other registrants are supporting the use, it should not be assessed.

HED Response:

This attached Quantitative Usage Analysis has been revised. A header has also been added to this table.

16. Page 47, Untitled Table: In the same table, the column under “Lb. AI applied”, for “Wtd Avg.”, it is unclear where these values were derived. This should be clarified as to a source. Also, were these values used in the assessment?

HED Response:

This is an attached Quantitative Usage Analysis. The only values in this table that are directly used in the exposure assessment are the percent crop treated estimates. A header has been added to this table.

17. Page 48, Untitled Table: In the footnotes to the table, it would be extremely helpful for the Agency to provide the weighting rationale in detail so the process used is transparent.

HED Response:

This is an attached Quantitative Usage Analysis. To improve clarity, a header has been added to this table.

Attachment 3

Syngenta's Comments on EPA's November 15, 2000 "Atrazine: HED Product and Residue Chemistry Chapters" (Including the Tolerance Reassessment Summary) and the November 15, 2000 "Atrazine: Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine

Response to HED Product and Residue Chemistry Chapters Including the Tolerance Reassessment

Typographical Errors:

1. Page 3, 1st Paragraph, Line 3: Atrazine is not registered for use on wheat. Change "wheat" to "and in wheat fallow programs".

HED Response:

Corrected as per comment.

2. Page 33, 1st Paragraph, Line 4: Syngenta does not have wheat labeled as a target crop.

HED Response:

Corrected as per comment.

3. Page 34, 1st Paragraph, Line 7 & 9: G-27283 should be G-28273.

HED Response:

Corrected as per comment.

4. Page 35, 6th Paragraph, Line 1: The current maximum post application rate is 2 lb ai/A, so the 3 lb ai/A rate used in the metabolism study is 1.5X, not 1.2X. Same comment for sorghum on Page 36 3rd Paragraph.

HED Response:

Corrected as per comment.

5. Page 36, 3rd Paragraph, Line 8: "a" should be deleted from between the words containing and several.

HED Response:

Corrected as per comment.

6. Page 36, 3rd Paragraph, Lines 7-10: Sentence beginning with "Aminex A-4 chromatography" should be divided into two sentences as follows: "Aminex A-4 chromatography of the residue produced a peak (Peak 7) containing several components, one of which was identified as the lanthionine conjugate of atrazine. Peak 7 was also identified in forage as accounting for £11.3% TRR.

HED Response:

Corrected as per comment.

7. Page 38, Last Paragraph, Line 3 & 4: GC/ECD should read GC/NPD.

HED Response:

Corrected as per comment.

8. Page 39, 1st and 2nd Paragraph, Line 1: GC/ECD should read GC/NPD.

HED Response:

Corrected as per comment.

9. Page 41, 1st Paragraph, Line 3: "<" signs for high value in range cited should be deleted.

HED Response:

Corrected as per comment.

10. Page 41, 2nd Paragraph, Line 3 & 5: "<" signs for high value in range cited should be deleted.

HED Response:

Corrected as per comment.

11. Page 41, 3rd Paragraph, Line 5: "<" signs for high value in range cited should be deleted.

HED Response:

Corrected as per comment.

12. Page 41, 5th Paragraph, Lines 8 & 9: "<" signs for high values in ranges cited should be deleted.

HED Response:

Corrected as per comment.

13. Page 42, 1st Paragraph (top of page), Line 1 (2 entries): "<" signs for high values in ranges cited should be deleted.

HED Response:

Corrected as per comment.

14. Page 42, 2nd Paragraph, Lines 4 & 5: "<" signs for high values in ranges cited should be deleted.

HED Response:

Corrected as per comment.

15. Page 42, 4th Paragraph, Line 5: "<" signs for high value in range cited should be deleted.

HED Response:

Corrected as per comment.

16. Page 42, 5th Paragraph, Lines 2 & 5: "<" signs for high values in ranges cited should be deleted.

HED Response:

Corrected as per comment.

17. Page 42, 6th Paragraph, Lines 3 & 6 (two entries on each line): "<" signs for high values in ranges cited should be deleted.

HED Response:

Corrected as per comment.

18. Page 43, 7th Paragraph, Line 9: "triazine" should be replaced with "atrazine."

HED Response:

Corrected as per comment.

19. Page 64: Table A: Fallow weed control (and continued control…). The label specifies "may extend into following corn crop…) Also the rates are incorrect for this wheat-corn-fallow use; The table lists ND and SD use >7.5 pH is 1.5 lbs. maximum, not the 1.4 listed, and the <7.5 pH maximum is 2.0 lbs. not the 1.8 listed.

HED Response:

Corrected as per comment.

20. Page. 64: Table A: Guava: Maximum number of applications per season is listed as 8.0 when the label says "Do not apply more frequently that at 4-month intervals". This should be changed from 8 to 3 applications.

HED Response:

Corrected as per comment.

Comments with Regard to Content and Conclusions of the Product Chemistry Chapter:

1. Page 21, footnote 16: The footnote states "An enforcement analytical method must be submitted for a new impurity identified on the revised CSF (9-20-94)". Please note the current CSF for Syngenta Atrazine Technical is dated 3-1899 and was approved by EPA on 9-16-99. In the CSF, the "new" impurity is not new, it is cyanazine. Cyanazine was listed to cover possible crop-contamination at the manufacturing plant. However, cyanazine is no longer being produced, so it can be dropped as an impurity and a new method is not needed.

HED Response:

Corrected as per comment.

Comments with Regard to Content and Conclusions of the Residue Chemistry Chapter:

1. Page 35, 5th Paragraph (Nature of the Residue in Plants): The description of the metabolism of atrazine in plants should be modified to include glutathione conjugation as part of the overall metabolic pathway. Lines 4 and 5 would be more accurate with the following modification: "Atrazine undergoes extensive metabolism in plants including: N-dealkylation to form the chloro metabolites G-30033, G-28279 and G-28273; hydroxylation of parent or chloro metabolites to form G-34048, GS-17792, GS-17791, and G-17794; and glutathione conjugation by displacement of the 2-chloro moiety. Rearrangement and dealkylation of thio-conjugates or amination of parent or G-30033 forms CGA-101248." The remainder of the paragraph should remain the same "Lanthionine, lanthionine sulfoxide and glutamine conjugates…".

HED Response:

Corrected as per comment.

2. Page 39, 1st Paragraph, Last Sentence: Method 484 (MRID 40431365) has previously been submitted to the Agency.

HED Response:

Corrected as per comment.

3. Page 39, 6th Paragraph, Last Sentence: The Agency is requesting an analytical method for all four hydroxy atrazine metabolites. Based on metabolism study results in corn, sorghum and sugarcane, only the hydroxy atrazine (G-34048) and desethylhydroxy atrazine (GS-17794) are found in a quantity which would be measurable by an enforcement method with an LOQ of 0.01-0.05 ppm. Thus only those two moieties should logically be included in a tolerance enforcement method, since only they would be measurable.

HED Response:

If the registrant can demonstrate through available data that the only hydroxy compounds of concern, i.e., detected in significant quantities, are the hydroxy atrazine (G-34048) and desethyl hydroxy atrazine (GS-17794), EPA will reconsider the requirement for establishing a tolerance on all four hydroxy compounds and a supporting analytical method. Based on our brief review of the residue data for the hydroxy compounds from available metabolism studies, hydroxy atrazine (G-34048) and desethyl hydroxy atrazine (GS-17794) are all detected in plant commodities; however, the des isopropyl hydroxy atrazine compound has also been detected in metabolism studies.

4. Page 42, 6th Paragraph, "Wheat ": In the June 29, 1995 memorandum written by John Abbotts to Venus Eagle, Joseph Bailey, and Kathryn Boyle in response to previous reviews and the reregistration Data Call-In of 10/90, the Agency recommended under conclusion 3 that a radiolabeled field residue study in fallow/wheat which determined the ratio between combined residues of parent and chloro metabolites to total triazine residues would satisfy the magnitude of the residue requirement for wheat. According to this conclusion, determination of this ratio in hay should also satisfy the requirement for the magnitude of the residues in hay in lieu of an additional residue program for atrazine and metabolites in hay as outlined in this residue chapter.

HED Response:

HED has reevaluated the need for geographically representative studies in wheat hay in response to this comment. Residues of atrazine in wheat forage, the wheat commodity with the highest residues, were up to 1.11 ppm, yielding a tolerance of 1.5 ppm in wheat forage. HED believes that a tolerance in wheat hay can be supported using the residues in wheat forage corrected for percent dry matter. Correcting 1.11 ppm for the ratio of percent dry matter between wheat forage and wheat hay (Hay/Forage = 88%/25% = 3.5), yields estimated residues in wheat hay at 3.9 ppm. From this HED proposes a tolerance in wheat hay at 5 ppm. If the registrant disagrees with this proposed tolerance, geographically representative studies must be submitted to support a different tolerance.

A tolerance for the hydroxy metabolites on wheat hay is also required. HED has proposed a reassessed tolerance for the hydroxy metabolites of atrazine on wheat forage at 0.5 ppm based on existing field trial data. HED further proposes a wheat hay tolerance for the hydroxy metabolites of atrazine of 1.5 ppm. The registrant may otherwise submit field trial data for establishing tolerance level residues for the hydroxy metabolites of atrazine on wheat hay.

5. Page 43, 7th Paragraph: In the case of sugarcane processing, the Agency has concluded that the submitted processing study (MRID 43160504) was inadequate because only a 2X exaggerated rate (20 lb a.i./A) was applied. While a 5X (50 lb a.i./A) rate would normally be required, the label for both the AAtrex 4L and Nine-O products clearly indicate that applications in excess of 10 lb a.i./A may result in crop injury. A 50 lb a.i./A treatment rate will almost certainly result in crop injury and compromise the study.

HED Response:

HED agrees that it is unproductive to treat sugarcane at concentrations that would result in phytotoxicity and is dropping the requirement for a study at 5X the seasonal application rate. HED does recommend another processing study using crops incurred with as large residues as possible from application of as much atrazine is safe, as late in the season as reasonable. If residue concentration is not seen, such a processing study might also demonstrate a significant decrease in residues in sugar cane sugar that would allow increased refinement in future atrazine exposure assessments.

6. Page 50, Last Paragraph, Rotational Crops: Limited field trials can be conducted on the Foliage of Legume Vegetables Crop Group to set tolerances after the Agency reviews a draft protocol, since the requested study for limited trials in a single crop group is not a guideline study.

HED Response:

HED requests clarification as the registrant's point in this comment.

Comments with Regard to the Tolerance Reassessment Summary:

1. Page 58, Table C. Milk: The Agency has proposed a reassessed tolerance in milk of 0.10 ppm. The previous milk tolerance was set at 0.02 ppm based on parent atrazine only. It is unclear how the Agency arrived at this value. Metabolism and residue data and methodology submitted by Syngenta (formerly Novartis) should lead to the conclusion that the tolerance should remain at 0.02 ppm. The analytical Lower Limit of Method Validation (LLMV) of Analytical Method AG-496A is 0.01 ppm per each chloro triazine analyte. There were no detectable residues in USDA's Pesticide Data Program (PDP) database at an average Limit of Detection (LOD) of 0.0075 ppb. In addition, the Agency used a value of 0.005 ppm for milk in their dietary exposure assessment based on theoretical dietary burden calculations. Based on the Agency's dietary burden calculations and the results from a recently submitted 3-level feeding study in lactating cattle which was conducted to determine the transfer of ^{14}C-atrazine residues to milk (MRID 43934412), an estimated total triazine residue level of less than 1 ppb would occur in milk. Thus, the current tolerance value of 0.02 ppm should be more than adequate for milk.

HED Response:

The reassessed milk tolerance of 0.10 ppm is based on combined residues of atrazine and the chlorinated metabolites taken from an anmal feeding study in which milk was sampled and analyzed for atrazine and all of the chlorinated metabolites. The summed residues were <0.06 ppm based on detectable residues of diaminochlorotriazine (DACT) in milk samples at up to 0.03 ppm and residues of atrazine and desethyl atrazine and desisopropyl atrazine at the detection limit (<0.01 ppm) each from dairy cows fed atrazine at a 3.75 ppm feeding level. The theoretical maximum dietary burden (MTDB) for atrazine in the dairy cattle diet (based on tolerance level residues) is 5 ppm.. The ratio of the MTDB to the feeding level closest to the MTDB used in the animal feeding study is 1.3X. Residues of <0.06 ppm multiplied by 1.3X approximate <0.08 ppm, which has been rounded to 0.1 ppm for the tolerance level for residues of atrazine and the chlorinated metabolites in milk.

The tolerance in milk is set as an upper bound on legal residues in milk. It is based on residues detected from animal feeding studies and the maximum theoretical dietary burden for atrazine in the diets of dairy cattle. It is not based on actual monitoring data or anticipated residues as are used in the dietary exposure assessments. Necessarily, the tolerance is higher than any anticipated residues of atrazine in milk.

Response to Anticipated Residues and Acute and Chronic Dietary Exposure Assessments:

Typographical Errors

1. Page 2, 2nd Paragraph, Line 4: "sugar cane" should read "sugarcane" throughout the document

HED Response:

"Sugar cane" has been changed to "sugarcane."

2. Page 9, 1st Paragraph, Line 2: Two MRID numbers were repeated (1994; MRIDs 43395504 and 43395504).

HED Response:

Correction noted.

Comments with Regard to Content and Conclusions of the Exposure Assessments:

1. Page 5, 4th Paragraph, Lines 2, 3: The 70:30 pre- and post emergence ratio was correctly derived from the 1997 survey data. However, more recent survey data (1998 and 1999) indicates that this ratio can change slightly.

HED Response:

If the registant believes that a the 70:30 ratio is not correct, they should submit the ratio they propose to HED.

2. Page 6, 3rd Paragraph: It is unclear how BEAD calculated "average" and "maximum" percent of crop treated and the values obtained for corn. Please provide the sources of data and weighting process for percent crop treated.

BEAD Response:

BEAD is in the process of updating and documenting our methods for calculating typical and maximum %CT. We plan to present these at a SAP meeting in June or July of this year. Until then, if a stakeholder wants information about out calculations, they can refer to our recent science policy paper titled "The Role of Use-Related Information in Pesticide Risk Assessment and Risk Management," which describes how these calculations are made.

The paper can be found at: http://www.epa.gov/pesticides/ the link is in the middle column (titled "OPP Topics"), under the heading "Pesticide Use," in the first link, called "role of use info."

3. Page 7, 2nd Paragraph:In order to be consistent with the chloro residue value calculation in corn, the adjustment for the percent of pre-emergent use vs. post-emergent use (70:30) should have been applied to the calculations for determination of the levels of hydroxy metabolites.

HED Response:

The estimated hydroxy metabolites in/on corn are all from field trials in which atrazine was applied post-emergent. Since there are no pre-emergent data, the 70:30 ratio cannot be applied. The dietary exposure memorandum has been modified to include this fact.

4. Page 9, 3rd Paragraph, Line 1: The Agency used a residue value of 0.031 ppm for the combined hydroxy metabolites in sugarcane molasses. Based on the results of the processing study performed as part of the magnitude of the residues in sugarcane (MRID 43160504) the hydroxy-metabolites, G-34048 and GS-17794, were present at values of < 0.02 ppm (LLMV) and at 0.02 ppm (LLMV) respectively. Using ½ LLMV for G-34048, the combined residues of the two hydroxy triazines in sugarcane molasses is 0.03 ppm.

HED Response:

The value of 0.031 was based upon a more precise calculation of these two hydroxy-metabolites which were then corrected to 0.031 to represent the expected value for all four hydroxy-metabolites. However, HED agrees that the uncertainty of the calculation is such that 0.03 more correctly reflects our actual knowledge of the residues than does 0.031. Therefore we have amended the dietary exposure assessment as suggested.

5. Page 10, Wheat: Atrazine use in wheat fallow programs is limited to application on fallow ground with wheat being planted at least a year later. Based on the use pattern and studies conducted with ^{14}C-atrazine, no parent atrazine residues would be anticipated as a result of the label use.

HED Response:

Comment noted.

6. Page 10, 1st Paragraph, Line 6: The Agency states that “No metabolism study had been performed on wheat…”. However, Novartis submitted a metabolism study in which wheat was grown as a rotational crop following corn and sorghum (MRID

43016505). This study mimics the actual use of atrazine as a fallow application prior to planting wheat. A radiolabeled magnitude of the residue study is currently in progress and will be completed and submitted to the Agency in early 2002.

HED Response:

Comment noted.

7. Page 12, 3rd Paragraph, Line 4: The Agency indicates that a tolerance of 0.05 ppm in guava was used in the dietary assessment. The anticipated guava residue value in EPA's PD-1 document ("The Triazine Herbicides, Atrazine, Simazine and Cyanazine, Position Document 1, Initiation of Special Review" (PD-1) from the U.S. Environmental Protection Agency, dated November 9, 1994.) is 0.01 ppm and this value was used in all recent Syngenta assessments.

HED Response:

The value of 0.01 ppm was based upon the highest result found for parent in the field trials for guava when only parent atrazine was measured. No metabolism study on giuava has been submitted to HED to enable translation of results for parent atrazine to the total of parent plus the three chloro-metabolites. Lacking exact metabolism data, the current tolerance at 0.05 ppm is more consistent with the total chloro-metabolite residues that may be expected to occur. In addition, use of 0.05 ppm is consistent with the HED policy of using tolerance level concentrations in dietary exposure assessment when adequate field trials for estimation of dietary exposure do not exist.

8. Page 15, 3rd Paragraph, Lines 3 and 4: The Agency states that the "…highest residues were 1.11 ppm and 0.221 ppm…". Syngenta is unable to mathematically reproduce these values from Table B2.

HED Response:

One correction and two conditions are needed to reproduce the "combined" values in these tables. The correction is that 0.221 should be <0.221. The first condition is that values 1.11 and <0.221 are the combined totals from the other columns after correction for molecular weight. Thus, the value of 1.11 is the sum of 1.06 + 0.015(216/188) + 0.006(216/174) + 0.015(216/146). The value of <0.221 is the sum of 0.191 + 0.005(216/188) + <0.005 + 0.013(216/146). For the second condition, note above that the results at the LOD <0.005 are not corrected for molecular weight, because they are not exact measurements. The sum thus is not an exact sum at 0.221, but an inexact sum of <0.221. A few other sums were similarly wrong in this table and have been corrected. These tables were tables of data from the original field trials, but precisely because the sums are not exact, the average residues were actually not taken from these tables, but from modified

tables. In the modified tables each exact residue is listed with its value as corrected for molecular weight. All <LOD residues taken to be exactly at 1/2 LOD, or 0.0025 ppm (not corrected for molecular weight). The average results for the chronic assessment are calculated only from residues in field corn taken at 30 days PHI, except in the 2.0 pre-emergence treatment scenario, where results were only available at 60 days PHI. These tables have now been used in the dietary exposure memorandum in place of the tables previously used.

The HAFT is still based upon the same field trial, which was a 60 PHI sample in the 0.5 lbs ai/A pre-emergence and 2.0 lbs ai/A post-emergence treatment scenario. The HAFT has been recalculated as the average of 1.11 and 0.215 = 0.66. [The value of 0.215 is the exact sum of 0.191 + 0.005(216/188) + 0.0025(216/174) + 0.013(216/146).] This small difference does not change the final residues estimated in meat and milk. Because the data for the HAFT are not in the three tables now attached for estimation of average residues, an additional, similar table containing these results now been attached as a fourth table. This should make the calculations more transparent.

Attachment 4

Syngenta's Comments on EPA's November 30, 2000 "Atrazine. HED's Preliminary Human Health Risk Assessment for the Reregistration Eligibility Decision (RED)" and the October 20, 2000 "Drinking Water Exposure Assessment for Atrazine and Various Chloro-triazine and Hydroxy-Triazine Degradates"

Surface Water

Methodology Corrections:

In calculating the Seasonal and Annual Means, EPA developed regression equations to calculate total chloro-triazine levels from measured atrazine concentrations using only the finished water levels (Henry Nelson's "Drinking water exposure assessment for atrazine and various chloro-triazine and hydroxy-triazine degradates" dated October 20, 2000 pages 13-14). Syngenta's approach was to develop the equations based on both raw and finished water and believe that this is the best approach since many other Community Water Systems do not treat their water to the extent the CWSs in this study do. While all of the chloro-triazines behave similarly with many water treatment processes, Syngenta believes that raw data correlation should also be considered in developing the quarterly equations. The Syngenta equations using both raw and finished water are as follows:

1st qtr $y = (0.813 \pm 0.060)x + (0.145 \pm 0.053)$ ($R^2 = 0.614$, n = 118, df =116)

2nd qtr $y = (0.311 \pm 0.018)x + (0.303 \pm 0.076)$ ($R^2 = 0.617$, n = 182, df =180)

3rd qtr $y = (0.594 \pm 0.035)x + (0.360 \pm 0.075)$ ($R^2 = 0.643$, n = 162, df =160)

4th qtr $y = (0.803 \pm 0.064)x + (0.103 \pm 0.084)$ ($R^2 = 0.569$, n = 120, df =118)

Estimated seasonal and annual mean water concentrations included in the EPA preliminary assessment for VMS and ARP datasets were calculated by using the EPA quarterly equations to calculate total chlorotriazine residues following by a simple averaging of the residues over a timeframe. For the PLEX dataset, EPA used Syngenta strongly believes that a time weighting of the residue concentrations should be used, particularly for the Voluntary Monitoring Study (VMS) and the Acetochlor Registration Partnership (ARP) data sets, where samples have been taken more frequently during the use season and there are generally several samples in a quarter. In addition, when data exists for a CWS in multiple data sets (i.e., PLEX, ARP, VMS), these data sets should be combined before determining exposure. The sum of all data adds to the understanding of time dependent variability leading to a more robust and defendable assessment of exposure.

The use of the maximum seasonal or annual means should only be used to assess exposure for those timeframes, i.e. 90 or 365 days, respectively. They should not be used to establish long term exposure levels at CWS, where data exist over a longer, more appropriate, time frame. Since these data sets generally contain residue levels over a period of several years, an appropriate highest period mean covering the exposure period being addressed should be used where possible for chronic exposure assessments. This would greatly improve the validity of the exposure assessment presented in the EPA preliminary risk assessment. Additionally, the comparison of the 3-

month average concentration to a DWLOC based on a chronic toxicology endpoint is not appropriate.

To assess exposure more accurately using a deterministic approach, Syngenta has combined the three data sets (VMS, ARP, and PLEX) for the 25 CWS mentioned in EPA's review as well as those listed in Appendix E. A time weighting of each data point was then performed by assigning the residue value of a sample to each day going back one half of days to the previous sample date and forward one half of the days to the next sampling date. The time-weighted mean was then determined by adding the residue values for each day and dividing by the number of days in the period being determined. This result of this process was that several of the systems had 40 to 50 samples per year which gives better distribution of sampling events than the 20 to 30 in either ARP or VMS programs alone and provides for better characterization of exposure.

The resulting exposure assessments even using a deterministic methodology indicated that five CWS had time weighted annual means over the 12.5 ppb preliminary chronic level proposed by EPA for infants <1 year old using the new OW body weights, a 1000 fold safety factor, and an endpoint derived from LH surge suppression in sexually mature adult rats (see Table below). These CWS are Dearborn, MO (14 ppb), Hettick, IL (20 ppb), Palmyra-Modesto, IL (15 ppb), Salem, IL (14 ppb) and Shipman (20 ppb). None of these exceed the DWLOC for infants <1 year (90 ppb) determined by using a more appropriate toxicology endpoint and a 1000 fold safety factor. These 5 CWS serve a combined population of 12,000 people. None of the CWS had 5 year period means over 18 or 23 ppb (EPA calculated DWLOC values) for children 1-6. It should be noted that Shipman no longer provides drinking water from the source monitored. In 1999, it switched its water source to another surface water CWS, Alton, Illinois and the annual means have dropped well below any of the calculated DWLOCs. The period mean for Shipman for 1993-1999 is 6.58 ppb chlorotriazines.

A probalistic exposure using the same composite database is included in this submission and

<u>EFED Responses to Syngenta "Error" Comments on Atrazine</u>

Time weighted average issues:

Syngenta's comment:

> Syngenta believes that time weighting of the residue concentrations should be used, particularly for the Voluntary Monitoring Study (VMS) and the Acetochlor Registration partnership (ARP) data sets, where samples have been taken more frequently during the use season and there are generally several samples in a quarter.

EFED's Response:

There are some differences in using the simple average versus the time weighted average. The annual mean concentration values of parent atrazine for VMS and ARP presented in EFED's assessment are based on the time weighted average approach. To be consistent, EFED has modified the annual mean values of total chloro-triazines by using the time weighted average approach for the annual mean of parent atrazine with the annual regression equation.

Both VMS and ARP were sampled either weekly or bi-weekly during the use season, and sampled monthly other seasons. With the constant weekly or bi-weekly sampling, there will be little difference between the seasonal mean calculated by simple averaging and the time weighted seasonal mean. For the seasonal mean, EFED has done some preliminary comparisons on a few CWSs and found that the difference is not significant, with some arithmetic means being higher than their time weighted counterparts and some being lower. EFED will consider further re-calculation of time weighted seasonal means for the rest of the data in the next draft**.**

Pooling of three data sets (VMS, ARP and PLEX):

Syngenta's comment:

Syngenta has combined the three data sets and used time weighted averaging for 25 CWSs.

EFED's Response:

Ideally, to pool the different data sets, the study designs should be identical. Since EFED is not certain that all the controlled factors are identical for these thee data sets, it is possible that there are some design differences. The differences exist in (1) the number of sampled CWSs, (2) the sampling dates, and (3) the detection limits. If all three data sets were compatible, results from all the CWSs should be combined and not just those from the selected few. EFED therefore believes that the datasets should not be pooled.

Regression equation issues:

Syngenta's comment:

Syngenta's approach was to develop the regression equations for chloro-triazines based on both raw and finished water and believe that this is the best approach since many other Community Water Systems do not treat their water.

EFED's Response:

We don't know the exact numbers of CWSs that did not treat their water. Considering that most of the CWSs are treating their water, it would be a better representation to derive the regression equations based on the finished water only. Therefore, the finished water values are used in the risk assessment.

Specific Comments on Preliminary Human Health Assessment:

1. Page 11, 3rd Paragraph, Line 6: In the list of 25 CWS, Iberville and Chariton (both listed in IL) are actually located in LA and IA, respectively.

2. Page 66: The population served by the Higginsville, MO CWS, as noted in PLEX was 4,700 not 10,000 as listed in Table 11.

3. In Appendix E the following items identified "Gerome", IL should be Jerome, IL.

4. The seasonal (3 month) means for Illinois CWS in the 1993 VMS as presented in Table 14 are based on one sample in June and was not calculated based on weekly concentrations from May to July (page 58). The VMS program was initiated in June, 1993.

5. Page 61-62 (Table 11); The chlorotriazine seasonal mean concentration of 22.29 ppb is incorrect. The highest seasonal mean in the composite database for Higginsville in 1996 is 2.29 ppb.

6. White Hall, IL switched from surface water to a ground water source in 1997. The annual atrazine mean form groundwater was 0.48 ppb and 0.50 ppb, in 1998 and 1999 respectively. The total chlorotriazine period mean was 3.66 ppb.

7. Replace atrazine with total chlorotriazine in the following sections:
   Page 70: 1st Paragraph; Line 9
   Page 86: 5th Paragraph: Line 5
   Page 87: 1st Paragraph: Line 1
   Page 89: 2nd Paragraph; Multiple statements
   Page 91: 6th Paragraph; Line 2

8. Page 86: 1st Paragraph: Line 2: Replace variously 0.12% with variously 0.05%.

9. Replace measured with calculated or estimated
   Page 89: 2nd Paragraph: line 7
   Page 90: 2nd Paragraph: line 5

In reviewing the EPA equations presented on page 13 of Henry Nelson's "Drinking water exposure assessment for atrazine and various chloro-triazine and hydroxy-triazine degradates" dated October 20, 2000 the value for n differs from the Syngenta data set submitted to EPA. The equations derived using just finished water samples in the data set are presented below:

EPA Equations

1st qtr $y = (0.535 \pm 0.137)x + (0.223 \pm 0.096)$ (Fig 3-3; $R^2 = 0.502$, n = 59, df = 57)

2nd qtr $y = (0.394 \pm 0.051)x + (0.107 \pm 0.108)$ (Fig 3-4; $R^2 = 0.710$, n = 94, df = 92)

3rd qtr $y = (0.704 \pm 0.165)x + (0.123 \pm 0.180)$ (Fig 3-5; $R^2 = 0.482$, n = 77, df = 75)

4th qtr $y = (0.630 \pm 0.137)x + (0.122 \pm 0.124)$ (Fig 3-6; $R^2 = 0.582$, n = 61, df = 59)

Correct Equations consistent with the finished water data set and N values

1st qtr $y = (0.535 \pm 0.141)x + (0.223 \pm 0.099)$ ($R^2 = 0.502$, n = 59, df =57)

2nd qtr $y = (0.402 \pm 0.050)x + (0.083 \pm 0.106)$ ($R^2 = 0.740$, n = 91, df =89)

3rd qtr $y = (0.661 \pm 0.167)x + (0.156 \pm 0.181)$ ($R^2 = 0.439$, n = 81, df =79)

4th qtr $y = (0.627 \pm 0.142)x + (0.126 \pm 0.130)$ ($R^2 = 0.576$, n = 60, df =58)

Syngenta's comment:

Syngenta raised the issue on the number (n) of samples used in generating the regression equations based on the finished water

EFED's Response:

EFED had used the numbers of 59, 94, 77, and 61, respectively for the first through the fourth quarter, whereas, Syngenta used the numbers of 59, 91, 81, and 60, respectively, to derive their four quarterly regression equations. There is still considerable data scatter around each regression line. Comparing the r^2 values of 0.48 to 0.71 (EFED's approach) to the r^2 range of 0.44 to 0.74 by Syngenta, there is no significant improvement in the Syngenta equations. EFED does not believe that adopting Syngenta's proposed approach will enhance the assessment.

Community Water System	State	EPA Review Highest Residue Found (ppb)	EPA Review Highest Annual Average (ppb)	Syngenta Highest Annual TWM for Combined Data (ppb)	Syngenta Period TWM for Combined Data (ppb)
Shipman	IL		24.8	20.5	6.6
Hettick	IL		22.9	19.1	8.4
Palmyra-Modesto	IL		18.5	15.0	4.7
Salem	IL	89	20.4	14.2	3.9
Dearborn	MO		14.3	13.8	4.3
Sardinia	OH	55.2	15.0	11.5	2.8
White Hall	IL		12.1	10.9	3.7
Holland	IN			10.2	2.8
Paris	IL	18.7		10.2	3.0
Gillespie	IL	69.1	12.6	9.4	3.7
Scottsburg	IL			9.3	2.6
Vermont	IL	17.3		9.1	2.3
Higginsville	MO			9.1	2.8
Osawatomie, Miami Co RWD #3	KS	17.3		9.0	3.3
Batesville	IN			8.5	3.8
Farina	IL			8.3	4.6
Bucklin	MO			7.5	1.8
Adrian	MO	22.9		7.0	1.7
ADGPTV	IL			7.0	3.5
Keysport	IL	18.7		6.9	4.0
West Salem	IL			6.7	3.9
Sorento	IL			6.7	2.9
Hillsboro	IL		12.2	6.1	3.0
Centralia	IL			6.1	3.3
Springfield	IL	20.1		5.9	2.4
Lake of the Woods, Sunbury	OH	18.1		5.8	4.0
Chariton	IL		2.0	5.8	2.3
Delaware	OH	19.8		5.8	3.2
Carlinville	IL			5.6	2.5
Wayne City	IL			5.6	1.6
North Vernon	IN			5.5	2.2
Iberville	LA			5.3	3.2
Vandalia	MO			5.0	2.8
Louisville	IL	24.3		5.0	3.5
Butler	MO	18.7		4.5	1.4
Kinmundy	IL			4.3	2.5
Clay City	IL	18.7		4.3	1.8
Three Rivers	IN	20.1		4.0	1.3
Flora	IL			3.8	2.6
Waverly	IL			3.8	2.7
Newark	OH	29.7		3.5	1.5
Napoleon	OH	17.9		3.3	2.5
McClure	OH	20.1		2.1	1.7

Groundwater Comments

HED's Preliminary Human Health Risk Assessment

1. Page 10, 12, 67: In the Rural Well Survey conducted by Ciba-Geigy Corporation during the period from September 1992 to March 1995, 8 out of the 1505 total surveyed wells (0.53%) had atrazine concentrations ³3 ppb, i.e., the first 8 wells in Table 1 (17491-KS-017, 17491-KS-068, 17491-MN-003, 17491-WV-033, 17491-IN-050, 17491-WI-080,17491-WI-045, 17491-WI-060). Six wells (0.40%) including 2 wells in the 8 highest atrazine wells (i.e. 17491-WI-045 and 17491-WI-060) exceeded the total chloro- atrazine 12.5 ppb, the chronic DWLOC for infants based on the new body weights recommended by EPA Office of Water (OW). Two wells had total chlorotriazine residues approaching 12.5 ppb (i.e., 17491-WI-092 and 17491-WV-019). However, only one well (0.066% of the total) in the entire survey (17491-WI-045) was slightly exceeding the EPA HED total chlorotriazine chronic DWLOC (18 ppb) for infants.

   Follow-up investigation, by Ciba-Geigy Corporation, of the 8 wells with the highest atrazine detections indicated that point source contamination might have contributed to the higher than expected concentrations of atrazine. Among the 8 wells, two were not used for drinking water. The deethylatrazine to atrazine ratios (DAR) in 8 wells were all significantly below unity (Table 1), indicating that the parent atrazine might have moved to ground water preferentially from point sources (Adams, C.D., and E. M. Thurman. 1991: Formation and Transport of Deethylatrazine in the Soil and Vadose Zone. J. Environ. Qual. 20:540-547). Under normal leaching conditions, atrazine degrades to DEA resulting in a larger DAR when residues are found in ground water. DAR values should be larger than unity because deethylatrazine is the primary degradation product of atrazine and has a lower soil Koc relative to the parent.

   For the 8 highest total chlorotriazine wells (two approaching 12.5 ppb), one was not a drinking water well and three had no recorded use of atrazine at least for 5 years prior to the sampling dates in the area where the wells were located (Table 1).

   Since the majority of the sampling activities for the concerned wells listed in Table 1 took place during 1992 to 1993, the beneficial effect from the last major use rate reduction of atrazine during the 1993 season and thereafter was probably not fully reflected in this study. For example, subsequent sampling and analysis of the 2 wells in PA showed significant reduction in the concentration of atrazine plus its chlorinated metabolites, decreasing total concentration from 14 and 15 ppb to 7.6 and 6.8 ppb, respectively. The two WI wells, 17491-WI-084 and 17491-WI-092, showed reductions in

atrazine concentrations from 2.3 and 1.0 ppb in 1992 to 0.32 and 0.58 in 1996, respectively. In these same wells, the total chlorotriazines were reduced from 13 and 12 ppb to 3.13 and 3.71 ppb, respectively during the same time period. Given that the survey was designed with well selection criteria strongly biased toward worst-case atrazine detections such as 1) previous history of detect(s), 2) high hydrogeological vulnerability, and 3) proximity to field with atrazine application history, the rural well data are not appropriate for a population-based regional/national scale drinking water assessment.

Groundwater issues:

Syngenta's comment:

Syngenta claimed that possible point source contamination was the reason that a total of eight wells (out of 1,505 wells sampled in the Rural Well Survey) had atrazine concentrations exceeding the MCL of 3 ug/L and one well with a total chloro-triazine concentration exceeding the chronic DWLOC of 18 ug/L for children and infants.

EFED's Response:

EFED stated in the drinking water memo that the Rural Well Survey is likely to have the most negative bias due to inadequate sampling frequency (only one sample per well). As the ARP groundwater monitoring results, showing that the monthly variation can be significant, which has relevance for the uncertainty in the results of the rural well study.

Syngenta's comment:

The Ciba/Syngenta PLEX update IV contains information on atrazine detection in rural non-community system wells in 21 major atrazine use states.

EFED's Response:

PLEX IV estimates a population of 15-17 million residing in these 21 states was not served by CWS and presumed this population is served by individual wells. According to the PLEX IV, the mean atrazine concentration of 0.154 ppb for 11,122 CWSs from groundwater in 17 major use states is higher than the mean atrazine concentration for rural wells from all of the four multi-state studies. The rural well studies have mean atrazine concentrations of 0.152 ppb (Novartis Rural Well Study), 0.058 ppb (USGS/NAWQA Study), 0.037 ppb (USGS/Mid-continent Study) and 0.057 ppb (Farm Bureau/Heidleburg College Study) based on the respective number of major

use states monitored in each study. Since the mean concentration of atrazine for the Novartis Rural Well Study is compatible with the mean of 11,122 CWS of groundwater source, the risk assessment results based on the rural well study for the groundwater drinking water source should be applicable to the 11,122 CWSs in 17 major use states from groundwater sources.

Table 1.

Well ID	County	Sampling Date	Atrazine (ppb)	Total chloro- (ppb)	DAR	Well Use	Year Well Bored	Well Depth (ft)	Distance to Field (ft.)	Atrazine Last Used	Years Used
Wells exceeding 3 ppb atrazine but less than 12.5 ppb total chlorotriazine											
17491-KS-017	Harvey	34498	5.1	6.2	0.12	OTH	1976	35	75	1994	90-94
17491-KS-068	Washington	11/30/94	3.8	4.5	0.16	D/O	1977	78	150	1991	90-91
17491-MN-003	Winona	08/23/93	3.4	5.6	0.41	D/O	1940	285	70	1993	93
17491-WV-033	Jefferson	09/13/93	4.2	6.3	0.24	OTH	1960	160	2640	1993	89-93
17491-IN-050	Jasper	8/19/93	9.1	11	0.15	DOM	1963	18	150	1992	90, 92
17491-WI-080	Dane	11/24/92	4.3	6.4	0.28	DOM	1920	60	Unk	1989	89
Wells exceeding both 3 ppb atrazine and 12.5 ppb total chlorotriazine											
17491-WI-045	Sauk	10/13/92	12.0	19	0.39	DOM	1972	150	50	1988	88
17491-WI-060	Sauk	10/28/92	7.0	13	0.67	DOM	1952	95	40	Not	Not
Wells exceeding or approaching 12.5 ppb total chlorotriazine but less than 3 ppb atrazine											
17491-WI-084	Richland	33938	2.3*	13*	2.00	DOM	1986	46	850	Not	Not
17491-WI-092	Dodge	12/7/92	1.0**	12**	2.50	DOM	Unk	75	100	NA	NA
17491-WV-019	Jefferson	8/9/93	0.96	12	3.44	DOM	1978	140	80	1993	89-9*3*
17491-WV-039	Jefferson	9/14/93	0.69	14	3.77	OTH	1955	20	300	1993	89-93
17491-PA-105	Franklin	6/28/93	1.4	15	3.57	D/O	1960	240	15	1993	89-9*3*
17491-PA-106	Franklin	6/28/93	1.7	14	2.76	DOM	1943	160	35	Not	Not

DAR = Deethylatrazine to Atrazine Ratio; D/O = Domestic or Other; DOM = Domestic; OTH = Other.
Atrazine Last Used = Year atrazine was last used at the sampling location.
Years Used = Years atrazine was used in the five years preceding the time of sampling at sampling location.
Not = Atrazine not used.
NA = No information available on atrazine use.
* Concentrations reduced to 0.32 ppb for atrazine and to 3.13 ppb for total chlorotriazine after resampling August 5, 1996.
** Concentrations reduced to 0.58 ppb for atrazine and to 3.71 ppb for total chlorotriazine after resampling August 6, 1996.

2. Page 53 & 54: Seasonal mean concentrations should not be used for comparison to chronic DWLOC values because the chronic DWLOCs were derived based on longer duration of daily exposure.

HED Response:

At a HIARC meeting subsequent to the release of the preliminary risk assessment [December 21, 2000], it was concluded that, although the endpoint selected for intermediate-term exposure of infants, children, young adults, and adults is derived from a 6-month study, it is reasonable to consider for an intermediate exposure duration, because data from a one month study showed effects on LH surge at 2.5 mg/kg/day after one month of dosing [from nonrepeat bleed measures]. Additionally, the intermediate exposure period is defined as 30 days to several months.

Drinking Water Exposure Assessment

3. Page 81: Table 8-1 provided percentile values of atrazine in ground water based on ARP Groundwater Monitoring Study for the period from May 1995 to March 1998. We could not verify the accuracy of the table because we do not have access to the ARP data.

HED Response:

Comment noted. Syngenta may want to request access to portions of the ARP database that affect atrazine.

4. Page 88: Eight wells (out of 1,505 wells sampled in the Rural Well Survey) had atrazine concentrations exceeding the MCL of 3 ug/L. As in the discussions above, follow-up investigations for the eight wells shown high possibility of point source contamination causing the detection of relatively high atrazine concentrations in these wells.

HED Response:

Any additional, follow-up data that will resolve some of the uncertainties associated with the limited sampling program for the rural wells will be welcomed and considered.

5. Page 89: Only one well (out of 1505 sampled in the Rural Well Survey) had a total chlorotriazine concentration equaling the HED sub-chronic/chronic DWLOC of 18 ppb for the chronic exposure of children and infants. As indicated in the follow-up investigation, this well likely had a point source contribution to the detection of high atrazine concentration (>3 ppb). Among the 6 wells with atrazine < 3 ppb but with total chlorotriazine greater than or

approaching 12.5 ppb, some of the wells had re-sampled results showing both reduced atrazine and total chlorotriazine concentrations far below 12.5 ppb (e.g., 17491-WI-084 and 17491-WI-092). Although no follow-up sampling data are available for the few other wells, they were either not drinking wells or located in areas of no recorded atrazine use for at least 5 years prior to sampling. The high chlorotriazine metabolite concentrations in these wells, thus cannot rule out possibilities of historical point source contamination in these areas, since a high level of atrazine might have degraded to chlorotriazine metabolites in the interval between last contamination and sampling.

Finally, results from the National Alachlor Well Water Survey (L. Holden and J. Graham et. al., Environ. Sci. Technol., Vol. 26, No. 5, 1992, 935-943) indicated that the MCL exceedance frequency of atrazine in private, rural domestic wells was less than 0.1% which is 5 times lower than the results from the Ciba Rural Well Study (i.e., 0.5%). The National Alachlor Well Water Survey was conducted in 1987-1989 with a statistically designed sampling method for well selection to represent approximately 6 million private rural wells in corn and soybean production areas in the United States. Ciba/Novartis PLEX database also contains information on atrazine detection in rural non-community system wells in 21 major atrazine use states. The PLEX database indicated that atrazine was detected above 3.0 ppb in only 0.15% of private rural wells (25 out of 16,382) which is very similar to the results from the National Alachlor Well Water Survey

HED Response:

Clearly additional sampling at those rural wells with levels of atrazine residues of concern, i.e., > 12.5 ppb would greatly improve the risk estimates for that portion of the population using rural wells for drinking water. HED welcomes additional monitoring and historical data on these 8 wells of interest. HED recognizes that these rural wells have been targeted for high-end atrazine exposures, and has indicated this in the risk assessment. That is, the 1505 wells in the Rual Well Survey represent rural wells with high-end exposure to atrazine residues and do not necessarily represent national exposures to atrazine residues in rural wells, i.e., in areas where atrazine is not used.

Comments on the Agency's Citation of the Laboratory, Aerobic Soil Metabolism Half-Life Values

In the Agency's October 20, 2000 document entitled "Drinking Water Exposure Assessment for Atrazine and Various Chloro-triazine and Hydroxy-triazine Degradates," the EPA notes on page 6 that the aerobic laboratory half-life value of atrazine is 3 to 4 months. This half-life value is further noted to have been derived

from "…several aerobic soil laboratory studies…" However, the reference(s) for these studies is not provided.

In February 1994, Ciba-Geigy Corporation (now Syngenta Crop Protection, Inc.) was notified in a "Grassley-Allen" letter from the EPA that the Agency was considering initiation of a Special Review of the major triazine herbicides (atrazine, cyanazine, and simazine) based upon potential human health and ecological effect concerns. On November 23, 1994, the EPA began the Special Review by publishing "Atrazine, Simazine And Cyanazine; Notice of Initiation of Special Review" in the Federal Register (EPA, 1994). This notice indicated that even though ecological effects were not a trigger in the Special Review, which was based upon human health concerns at that time, the EPA was nonetheless concerned about atrazine residues "…because they may have the potential to cause effects on aquatic organisms and terrestrial plants and their ecosystems."

To address the concerns of the EPA, and to respond to the request for additional information, Syngenta formed a multi-disciplinary expert panel to conduct a comprehensive and updated ecological risk assessment of atrazine. The assessment would build upon the existing atrazine ecological risk assessments (Solomon, et al., 1996; Fairchild, et al., 1994) incorporating data collected through 1999. The panel, named the Atrazine Ecological Risk Assessment Panel, was comprised of ecotoxicologists, environmental chemists, and modelers from academia and independent consulting organizations in the United States and Canada. In response to the needs of the Panel, Syngenta conducted a review of pertinent physicochemical and environmental data of atrazine to provide the Panel with a more accurate and reliable data to be used for higher tier modeling of atrazine. The Panel's report (Giddings, et al., 2000) summarized the environmental fate data on atrazine based on extensive literature search and review of in-house data available from Syngenta. The following information concerning the aerobic soil metabolism of atrazine is excerpted from the Panel's report.

Aerobic Soil Metabolism Half-Life Value (Laboratory)

Extensive research has been performed over the past thirty plus years to determine the fate and persistence of atrazine. Approximately seventy references, including studies available in the public domain, summaries, books, and unpublished studies, were evaluated for potential data on the transformation of atrazine. Research performed on soil in a controlled, laboratory environment under similar experimental conditions was the focus of the search. Six studies, representing ten unique atrazine half-life values, were considered representative of the dissipation of atrazine. These values are presented in Table 1. Numerous studies were not considered for the following reasons; extremes in experimental conditions, e.g., temperature and soil moisture; the soil was fabricated in the lab (vs. field collected); the soil was amended with bacterium or an energy source; the study was an outdoor, field study; or, the analytical procedure, extraction method, and/or,

detection limits did not generate acceptable results. The half-life values in Table 1 ranged from 20 to 146 days with a mean value of 44 ± 38.6 days.

If two or more laboratory values are available, the USEPA uses the following equation to calculate a conservative half-life value for use in exposure modeling (USEPA, 1995):

(Equation 1) $t_{1/2}$ (days) = $x + t_{90}[s/(n)^{1/2}]$

in which $t_{1/2}$ is the half-life in days used in the model, x is the sample mean in days, t_{90} is the *t*-test value at 90% confidence, *s* is the sample standard deviation, and *n* is the sample size. Calculations are performed on the half-life as opposed to the rate constant (day^{1}). The resultant approaches the mean as the sample size increases. Decay rates in surface soils were calculated using reported aerobic soil metabolism half-lives for the ten values summarized in Table 1. Using the t-test equation, the aerobic soil metabolism half-life was estimated as 61 days.

Syngenta Crop Protection recommends that EPA use the mean aerobic soil metabolism half-life value of 61 days that was reported by the Atrazine Ecological Risk Assessment Panel in their Expert Panel Report. Syngenta requests the use of this value instead of the value noted in the Agency's October 20, 2000 document entitled "Drinking Water Exposure Assessment For Atrazine And Various Chloro-triazine And Hydroxy-triazine Degradates."

Aerobic soil half-life:

Syngenta's comment:

> Syngenta will be sending data to support a mean value of 61 days, rather than the three to four months mentioned in EFED's Drinking Water Assessment.

EFED's Response:

> A detailed evaluation of data considered by EFED, including aerobic soil metabolism data, is presented in the Environmental Fate & Effects Chapter, which was submitted one week following submission of the DW Assessment. EFED will review any additional studies Syngenta sends.

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10. U.S. Environmental Protection Agency, "Input Selection For Computer Modeling of Aquatic Pesticide Exposure Using The PRZM2 And EXAMS II Programs," Version 1.1, June 1995.

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Table 1. Aerobic Laboratory Soil Metabolism

Soil Texture Class	Soil Series	Soil Origin	% Soil Moisture[a]	Soil pH	% Soil OM	Study Temp (°C)	Study Rate (ppm)	Half-life (days)	Ref.
Sandy Loam	Hanford	CA	12	6.05	0.74	25 ± 1	10	26.6	Singh, 1990
Loamy Sand	Tujunga	CA	4	6.3	0.57	25 ± 1	10	22.9	Singh, 1990
Silt Loam	Falaya	TN	80 (FMC @ 1/3 bar)	5.5	0.66	25	5.6	21	Winkelmann, 1991
Silt Loam	Falaya	TN	80 (FMC @ 1/3 bar)	5.5	0.66	25	1	20	Winkelmann, 1991
Sandy Loam	Cape Fear	NC	80 (FMC @ 1/3 bar)	5.3	5.1	21 ± 2	1	59.3	Blumhorst, 1994
Loam	Les Evouettes	Switzerland	75 (FMC @ 1/3 bar)	6.8	6.38	20	10	56.4	Abildt, 1991
Loam	NR	CA	75 (FMC @ 1/3 bar)	7.6	1.4	25 ± 1	10.2	146	Nelson, 1991
Silty Loam	NR	Germany	60 (MWHC)	5.1	2.2	25	5	39.4	Qiao, 1996
Silty Loam	NR	Germany	60 (MWHC)	7.6	1.8	25	5	24.9	Qiao, 1996
Sand	NR	Germany	60 (MWHC)	4.1	3.8	25	5	23.8	Qiao, 1996
							Mean:	44	
							Std. Dev.:	38.6	
							N:	10	
							Median:	25.8	

[a] Soil moisture during incubation.
FMC = Field Moisture Capacity.
OM = Organic Matter.
MWHC = Maximum Water Holding Capacity.
NR = Not reported.

Attachment 5

Syngenta's Comments on EPA's November 15, 2000 "Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Atrazine"

Detailed Comments on: Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Atrazine

1. Page 4, 2nd Paragraph, Line 8: Syngenta disagrees with the maximum acres used by EPA for aerial application (See Comment 8 below).

HED Response:

The acreages used for the aerial applications to various crops are based upon information obtained from reliable sources, including the National Agricultural Aviation Association (NAAA), the USDA and their extension agents, and various grower groups and crop protection associations. The aerial acreages used are not the highest possible for a crop, nor do they represent use of the largest or fastest equipment available. The acreages used are an approximation, based on the cited data, of a reasonable high-end day of aerial application to that specific crop. The specific references used are contained in the HED Science Advisory Council (SAC) for Exposure policy memo on "Standard Values for Daily Acres Treated in Agriculture," which was last revised July 5, 2000. These SAC "policies" are actually internal Agency SOPs designed to improve and update the science, and enhance consistency and accuracy in the published exposure and risk assessments. While the policies and SOPs are a reference for initial risk assessments, the values can be adjusted based on receipt and review of chemical-specific data. These data include usage information (small or large users; total lbs applied in state or US per annum, etc.), geographic variation (e.g., hilly, flat, small individual fields), dilution factors (high dilution = less chemical applied per day), etc., which may be supplied by multiple interested parties. (Comment 8 refers to fertilizer production.)

2. Page 4, 4th Paragraph, Line 3: Triming/harvesting of Christmas trees occurs several months after application (see comment 8 below) and there is a 30 day restriction on sod lifting, therefore the use short term dsildgeable foliar rsidues in inapproopriate.

HED Response:

The Agency consulted with its experts including the Biological and Economic Analysis Division (BEAD) and agrees in principle with Syngenta's statement. Because all of the reentry exposures are not fully understood, and additional information is being sought, all of the postapplication worker exposure calculations for conifers and Christmas trees will be included for characterization purposes. Note that all risk estimates for the postapplication workers do not exceed HED's level of concern (MOE s are greater than 100 on the first day after treatment).

3. Page 5, 1st Paragraph, Line 5: The "Standard Operating Procedures (SOPs) for Residential Exposure Assessment" revised December, 1999 is referenced several times in this document, yet this revised document does not seem to be available to the public.

HED Response:

The "Draft Residential SOPs" were initially published in 1997 and have undergone considerable scrutiny, research, and discussion since then. As noted above, all of the Agency SOPs are intended to provide guidance for more consistent, accurate risk assessments. Several proposals for changes to the "Residential SOPs" were presented to the Science Advisory Panel in December, 1999, based on recent observational and experimental studies related to residential exposure. The refinement of these proposed changes were based on SAP comments, continued research, and discussion within the Agency and specifically within the Exposure SAC. A summary of the "revised, draft Residential SOPs" is currently being produced and will be provided to interested parties as soon as review is completed.

4. Page 5: 1st Paragraph: The summary of residential handler exposure and risk estimates states that there are some scenarios that have short-term risks of concern; this contradicts the information displayed in Table 16a and discussed on page 45. When the lower quality, low confidence PHED data for hose-end and low-pressure handwand data are used, the MOEs are below 1000. However, when using the higher quality, larger database of ORETF data, the MOEs are well above 1000. This higher quality data, which was submitted to EPA in November, 1999, by the Outdoor Residential Exposure Task Force, should be used to assess exposure to residential handlers. This is acknowledged by EPA on page 45: "The recently submitted ORETF exposure study data for push type granular spreader and hose-end sprayer had greater numbers of replicates and therefore greater statistical power than studies previously used in PHED. Therefore, in the absence of atrazine-specific data, the ORETF data will be used for these two scenarios." In light of this conclusion, only the highest quality data should be used to assess risks to atrazine; the statement that two use scenarios are of concern on page 5 is inaccurate and should be revised.

HED Response:

In the revised preliminary risk assessment, the ORETF data for hose-end sprayer were adopted in lieu of the PHED v. 1.1 data. No ORETF data are available for the low pressure hand wand or backpack scenarios. Therefore the PHED data-based calculations are cited. The atrazine granular formulation push-spreader applicator study data is included in the risk assessment, as it is chemical-specific. Further refinement of the surrogate chemical database, including incorporation of ORETF and other values, is in progress.

Note that the risk estimates for residential handlers do not exceed the level of concern in the revised preliminary risk assessment. Additional usage data, such as gallons used or acreage treated per day, could refine the current daily use rate assumptions and affect total exposure estimates. Label instructions limiting use of the liquid formulation to spot-treatment would help reduce the risks for low-pressure handwand and hose-end sprays as they would not be intended for application to an entire lawn.

5. Page 5, 2nd Paragraph, Line 1: The post-application risks to liquid treated turf are summarized, but the post-application risks to granular treated turf are missing. These should be summarized here too. Also, please specify that acceptable MOEs exist for adults golfing and mowing <u>on both liquid treated and granular treated turf</u>; currently the type of formulation is not stated. Again, please specify the formulations types that result in acceptable MOEs for incidental turf mouthing and soil ingestion.

HED Response:

The results will be clarified in the revised document.

6. Page 5, 4th Paragraph, Line 2: In the second sentence, please specify that the short-term dermal for <u>liquid treated</u> turf and short-term hand-to-mouth (liquid and granular treated turf) exposures have MOEs less than 1000.

HED Response:

The results will be clarified in the revised document.

7. Page 6, 4th Paragraph, Line 1: The impregnation of atrazine onto dry fertilizer is a highly specialized process that requires large-scale commercial equipment, and does not occur “on-farm”. This reference to on-farm treatment needs to be deleted throughout this document. Syngenta will submit a document in January that details the herbicide impregnation

process so that the risks can be more accurately assessed.

HED Response:

The Agency encourages submission of additional information to clarify this exposure scenario. The Agency believes, at a minimum, individual farmers may apply treated fertilizer, and encourages submission of information about daily acres fertilized and equipment used.

8. Page 6, 4th Paragraph, Line 4: In response to EPA's request for more information regarding atrazine spray practices and postapplication activities on conifer forests and tree farms, Dr. Michael Newton from the Forest Science Department, Oregon State University, College of Forestry, Corvallis, Oregon was contacted. The information he provided is representative for the states of Oregon, Washington, and, California which are the primary forestry states.

Current use of atrazine in the forestry industry is minor. Major herbicides currently being used are Velpar and Oust because of their broader weed control spectrum.

Weed control is utilized in "Clear Cut" areas in the first two years of conifer establishment for faster release of seedlings. The size of clear cut areas varies, generally in the 20 to 80 acres range per area. In some states, there are regulations that limit the maximum size of each clear cut area. Atrazine application is normally made before or after planting in the spring.

The majority of herbicide application (~ 90%) is by helicopter. The tank capacity on a helicopter is less than in an airplane, and thus the standard load would be 100 gallons of spray solution, applied in a volume of 10 gallons of water per acre. The application rate of atrazine, if used, would be 4.0 lbs. active ingredient per acre. Based on a 100 gal load and 10 gpa, each load would treat 10 acres. On average, approximately 3 hours per day can be utilized for actual helicopter spraying, because of changing weather conditions, particularly wind speed. Considering the multiple "small" plots to be sprayed, the small load size, and the limited time frame per day, on an average day a pilot would treat approximately 150 acres; a high end estimate would be around 350 acres per day per pilot. It would be impossible for a pilot to spray 1200 acres per day.

The helicopter is loaded from a tank truck containing the pre-mixed "ready-to-spray" solution of water and herbicide. The transfer of spray solution from the tank truck to the helicopter is done through a completely closed system with the pilot having no exposure during the operation. The herbicide and water are mixed in the tank truck at another site and driven to the application

site in advance of the helicopter in order to minimize unproductive flight time from application sites to the mixing/loading site.

Christmas tree production was also discussed, and again, atrazine is not the major product. Velpar would be most commonly used. Most application would be aerial by helicopter, but the size of application sites are smaller, except for a few large plantations. Thus, total acres applied per day per pilot would be less than the reforestation site discussed above. In newly planted sites, application may be by ground equipment. Application is commonly done in the spring – mostly in March. Trimming or shaping of trees by hand is done after mid-July when annual growth is complete; harvesting of the trees is done in November and December, months after an atrazine application.

Based on this information, Tables 5, 6, 7, 8, and 9 need to be revised for conifer forests for mixing/loading liquids for aerial application, mixing/loading dry flowable for aerial application, and applying liquids with aircraft. The acreage assumption of 1,200 acres needs to be deleted. Using 350 acres represents an upper-end estimate of how many acres of conifer clear-cut areas that can be treated per day. Due to the limited clear-cut forestry acreage that can be treated with atrazine and the fact that atrazine is not used much in this industry, it is unlikely that a mixer/loader or a commercial pilot who services these geographic areas would spray atrazine for more than 7 days per year; thus there would be no need to assess intermediate-term risks for these scenarios.

HED Response:

The daily acreage treated for conifer forests has been revised to a reasonable high daily limit of 350 acres, and the risk assessment has been changed to reflect this number. The Syngenta information is welcomed, and confirmed by a range of 67-343 acres as "typical to high" from surveys by NAAA (data supplied electronically by the NAAA on January 2-4, 2000). The Agency is seeking further information from all sources, including the USDA Forest Service.

9. Page 6, 4th Paragraph, Line 4:The majority of atrazine that is applied to corn, sugarcane and sorghum is applied by ground, not by air. Acreage and pounds of atrazine applied by air in corn, sorghum, and sugarcane, are available at state level. For example, there are only 216,508 corn acres in the US having aerial application of atrazine. For sorghum there were 337,304 acres and sugarcane had 10,610 acres. These values are very small when considered as a percent of the total acreage treated with atrazine. When broken down to the state level, the acreage is substantially less. For instance, the least number of sorghum acres treated by air by state in 2000 (excluding those with 0 acres treated) are 340 (Nebraska) and the

greatest is 127,741 (Texas). For corn, the state reporting the fewest acres treated by air (excluding those with 0 acres treated) is New Mexico at 1,915 A and the most is Texas at 106,867 A. This indicates that it is extremely unlikely that a single aerial applicator would be spraying 1,200 acres per day for multiple days with atrazine. Thus, if the acreage assumption of 1,200 acres per day is used, there would be no need to assess intermediate-term risks since the use data show that it is highly unlikely that one pilot will be spraying more than 8,400 acres (1,200 a/day x 7 days) in a particular geographic region. The intermediate-term risk assessments in Tables 5, 6, 7, 8, and 9 need to be removed for corn and sorghum when 1,200 acres/day is assumed for mixing/loading liquids for aerial application, mixing/loading dry flowable for aerial application, and applying liquids with aircraft.

HED Response:

Please see also the response to Comment # 1. The acreages used are intended as reasonable high daily application rates. They do not represent maximum possible acreages, which data shows can be significantly higher for crops such as corn or sorghum. It is recognized that the high-end number of acres may not be treated every day, and it is highly unlikely that the high acreage estimate would apply to more than 30 continuous days for aerial applicators. These characterizations were includes in the draft exposure and risk assessment.

10. Page 6, 4th Paragraph, Line 4: There is no need to assess risks to human flaggers as they are no longer used in agriculture (need to cite a source of this info). Most spray planes and helicopters are equipped with GPS that allow the pilot to see where he has sprayed and where he needs to spray. Automatic drop flags from the aircraft are also sometimes still used, although most pilots use GPS.

HED Response:

The revised preliminary risk assessment assumes that human flaggers will not be used when treating very large acreage, and there are no risk estimates of concern for flaggers. The Agency agrees that most aircraft used for aerial application are now equipped with GPS or other means to determine the area to spray, and what has already been sprayed. The NAAA 1998 survey indicates about 60% of aerial applicators use a GPS control system, and 85% use some mechanical or electronic control system (only 15% use human flaggers). The survey shows that flaggers are still used in some instances and by some aerial applicators, predominantly pilot owner-operators . Atrazine labeling could stipulate use of GPS systems to eliminate hazards to human flaggers.

11. Page 14, 7th Paragraph, Line 1: Although it is stated on that risks for roadside application (including bermuda-grass) will not be done at 4 lb ai/A, they were assessed at this rate. Syngenta's labels do not support this rate; rather the risks should be assessed at the label maximum rate of 1 lb ai/A. Tables 5, 6, 7, 8, and 9 need to be revised to reflect this error.

HED Response:

The labels for this use do not clearly limit application to "roadsides" but instead "highway rights-of-way." There is no application equipment specified on the labels, so HED has used the closest equipment for which surrogate exposure data are available, which is commonly called the "right-of-way sprayer." There is little data on the equipment used or exposure information, so this is a best-estimate based on HED and BEAD experience. The labeled rates include, 1, 2, 2.2, and 4 lbs ai/acre and all are special local need (SLN) registrations. The 4 lbs ai/acre labels are still active but are dated 1985 and 1989. The Chemical Review Manager for atrazine is currently attempting to determine the need for continued registration of these SLN registrations, particularly at the higher application rates.

12. Page 15, 2nd Paragraph: Handler scenarios 1c, 2c, and 6 are incorrect. Atrazine is used for roadsides only, not rights-of-way (these include railroad tracks, power company land, etc). This needs to be corrected throughout the document and the tables.

HED Response:

The text has been clarified. See also the HED Response to Comment #11.

13. Page 15, 1st Paragraph, Line 4: It is correctly stated that mixer/loader/applicators would not require more than 1 week to treat their courses, and that this work is done by a golf course employee rather than a commercial applicator service. As noted, this same situation occurs on sod farms. As a result, short-term risks (1 to 7 days) need to be assessed, but intermediate-term (7 days to several months) do not. However, intermediate-terms risks were calculated for sod farm and golf course mixer/loaders and applicators in Tables 5, 6, 7, 8, and 9. These risks should be removed from the tables and from the discussions of the tables.

HED Response:

As stated in the text, the handler exposures are unlikely to exceed 30 days duration. However, the intermediate-term risk estimate is included until

sufficient atrazine-specific usage information is obtained for these applications.

14. Page 15, 1st Paragraph, Line 9: As noted, macadamia nut and guava orchards are of limited size and thus mixer/loaders and applicators applying atrazine in these orchards for weed control would handle the product less than one week. Based on data from the 1997 Census of Agriculture, there are 999 acres of guavas in Hawaii and 238 guava farms; there are 20,571 acres of macadamia nuts and 1,153 macadamia nut farms. The average farm size for these commodities is less than 20 acres. The standard default assumption that 80 acres are treated by groundboom per day is an overestimate for these crops. A more appropriate acreage should be used to assess risks to these workers and intermediate-term risks should not be calculated.

HED Response:

The Agency agrees that applicators treating these crops are probably exposed to atrazine for less than 30 days. Some farms exceed 80 acres. The Agency would like more information on the application methods for these crops, for instance to determine if groundboom or some other method (eg., truck-mounted spray) is used. Meanwhile, the HED will try to confirm these data with BEAD.

15. Page 15, 2nd Paragraph: Handler scenario (3), loading granular formulation, and (9) applying granular formulation with a tractor-drawn spreader, are not correct and need to be removed. Atrazine is not available as a straight granular formulation. It is only available on fertilizer, and this is covered by scenario (8). Atrazine impregnated bulk dry fertilizer is not bagged and, therefore, there is no conventional loading of granules. The treated bulk fertilizer is loaded into trucks at the fertilizer dealership. These trucks are either equipped with spreaders or they are driven to the field site and the material is transferred to application trucks.

HED Response:

The HED believes that granular (pre-formulated fertilizer) formulation may be applied by tractor-drawn spreader, particularly to turf or sod. Scenario (8) is specific to field crops such as corn and sorghum.

16. Page 15, 2nd Paragraph: As mentioned earlier, handler scenario (1e), mixing/loading/ incorporating liquid formulation into dry bulk fertilizer on-farm does not take place. Scenario (15), flagging for aerial spray applications does not take place either. These exposure scenarios should be removed.

HED Response:

See response to Comments 7 and 10.

17. Page 24, 2nd Paragraph: The ORETF mixer/loader/applicator exposure studies discussed by the agency are more appropriate for assessing exposure to lawn care operators than the chemical-specific atrazine study. The two exposure monitoring studies (turf handgun and push-rotary broadcast spreader) conducted by ORETF using volunteers from a large, nationally recognized lawn care company contain more replicates than the atrazine exposure study; were conducted using lawn care professionals as opposed to simulated LCO professionals; were conducted wearing clothing representative of clothing typically worn by LCOs; and the area treated/amount of chemical handled was more typical of LCOs. For these reasons, the risks summarized in Table 10 more accurately represent risks to the LCOs than do the scenarios (12) and (13) in Tables 5, 6, 7, 8, and 9. Scenarios (12) and (13) should be removed in favor of the more robust and higher quality data set that exists from the ORETF studies.

HED Response:

(See also the response to Comment #4) In the revised preliminary risk assessment, the risk estimates for all LCOs did not exceed the level of concern, after the addition of PPE. No ORETF data are available for the low pressure hand wand or backpack scenarios. Further analysis of liquid atrazine formulation labels revealed the dilution necessary to treat a single acre by pump spray or backpack (40 gallons) would be the reasonable maximum that could be mixed, loaded, and applied in one day. Therefore refined risk estimates were conducted using the PHED data set. The atrazine granular formulation push-spreader applicator study data is included in the risk assessment, as it is chemical-specific. The applicators were also wearing typical LCO clothing in this study. Further refinement of the surrogate chemical database, including incorporation of ORETF and other values, is in progress.

18. Page 26, 2nd Paragraph, Line 4: Please clarify that statement in the first paragraph under “Pesticide Handler Exposure Database” where it is stated that the agency is using PHED as a primary source of surrogate exposure data when a large data set of atrazine-specific monitoring data exists for the scenarios that are being assessed (mixer/loader for groundboom and closed-cab groundboom application to corn). It seems contradictory to use surrogate data when high quality chemical-specific biomonitoring data are available.

HED Response:

Exposure and risk estimates were made using both the atrazine-specific and PHED surrogate data. The quality of the data from both sources are discussed in the Agency's assessment. Study data provide good corroborative exposure estimates for "typical practices and levels of protection," but PHED was used, as is policy in HED, to present a range of exposure with increasing levels of personal protection or engineering controls.

19. Page 27, 8th Paragraph, Line 1: As discussed earlier, 1,200 acres per day for aerial application to clear-cut forestry plots is not realistic nor possible – this needs to be deleted from the conifer forest risk assessments.

HED Response:

See response to Comment #8.

20. Page 28, 4th Paragraph, Line 1: As discussed earlier, 80 acres per day for ground application to guavas and macadamia nut orchards is not realistic based on their small size. A more appropriate acreage based on census data should be used.

HED Response:

See response to Comment #14.

21. Page 28, 6th Paragraph, Line 1: As discussed earlier, flagging is no longer done.

HED Response:

See response to Comment #10.

22. Page 28, 7th Paragraph, Line 1: The estimate of 960 tons per day of bulk fertilizer being mixed and loaded is incorrect. This value is closer to 150 to 300 tons per day. As a result, the MOEs listed in Tables 5-9 are incorrect. Syngenta is in the process of gathering this information from various fertilizer dealers and will put together a document that describes the treating process in detail. This document will be submitted to the agency in January.

HED Response:

See response to Comments 7 and 15.

23. Page 28, 9th Paragraph, Line 1: The default assumption that professional LCOs spray 5 acres per day contradicts the default assumption of 3 acres

per day that the agency used in its June 1, 2000, atrazine occupational and residential risk assessment. The ORETF did not provide information to support 5 acres per day are treated by LCOs; the data provided by ORETF supported 2.5 acres per day as a high-end estimate. For an upper-bound estimate of area treated and to be consistent with how the agency is conducting similar risk assessments for other turf products, the default assumption of 3 acres per day should be used.

HED Response:

Note that in the revised preliminary risk assessment, all LCO risk estimates do not exceed the level of concern (MOEs are greater than 100) with gloves. Syngenta apparently is referring to another chemical, as there was no June 1, 2000, atrazine assessment. The ORETF recommends 2.5 acres treated per day, per LCO applicator, as typical. However, the Agency has presented both 3 acres/day ('typical') and 5 acres/day ('maximum') in the diazinon risk assessment. Use of 5 acres per day is consistent with a reasonable high-end daily handler exposure.

24. Page 29, 1st Paragraph, Line 3: The generic protection factor for a layer of clothing is 80 to 90%, not 50%. Data in PHED supports a higher protection factor as does the large data set submitted by ORETF where both inner and corresponding outer dosimeters were analyzed. Based on this information, the use of 50% protection overestimates potential exposure and should be revised.

HED Response:

The protection factors afforded by protective clothing vary greatly, but HED has adopted a 50% protection factor for a second layer of clothing, based on a wide variety of historical studies. In ideal conditions, such as cautious mixing and loading, much higher protection factors may be obtained. Applicators often are afforded much lower protection factors, for instance when spraying. The Agency is considering all data on this subject and currently is in the process of harmonization with the NAFTA values.

25. Page 29, 2nd Paragraph and continuing: As mentioned earlier, there are some assumptions in the atrazine impregnating scenario that are incorrect. First, this is a commercial process only; no on-farm fertilizer impregnation takes place. As noted by the agency, the common rates for application to corn and sorghum are 400 to 700 pounds per acre; lower rates than this result in poor distribution and are thus not typical. The assumption that the hourly put-through (tons/hr) can be simply multiplied by 8 hours per work day is erroneous. Fertilizer treatment is limited by blender capacity, applicator capacity, and the number of trucks that can be filled per hour. A facility would

be treating fertilizer with other pesticides during a day, not just atrazine. Therefore the assumption that 960 tons of fertilizer is treated with atrazine per day is a gross overestimate. As requested by HED, Syngenta will supply information and data regarding this use scenario in January.

HED Response:

The Agency welcomes additional data. See also response to Comments 7 and 15.

26. Page 35, 3rd Paragraph, Line 11: As mentioned previously, the maximum application rate for the roadside application is 1 lb ai/A. When 1 lb ai is used, the MOE is greater than 100. Please use the correct application rate.

HED Response:

See response to Comment #11.

27. Page 36, 1st Paragraph, Line 3: As mentioned previously, risks to LCOs should be assessed with the best data available – and this is the ORETF data. Comparison to the lesser quality PHED dataset adds no value and is confusing to the reader.

HED Response:

See response to Comment 17.

28. Page 36, 2nd Paragraph and Page 38: As indicated earlier, intermediate-term concerns for corn and sorghum mixer/loaders do not exist if it is assumed they are treating 1,200 acres per day by air. Aerial application to conifer forests are not made to 1,200 acres per day; assuming an upper-bound of 350 acres/day, intermediate-term concerns for mixer/loaders and applicators are resolved. Intermediate-term risks will be reduced for the roadside worker if the rate is changed to 1 lb ai/A.

HED Response:

See response to Comment #8.

29. Page 39, 2nd Bullet point, Line 1: The default number of days per year that commercial pesticide applicators and mixer/loaders handle any given product ranges from 15 to 30 days, depending on the pesticide in question. Based on the limited number of atrazine applications that can be made to one crop per year (typically one or two) and the data previously submitted by Syngenta that showed the average length of time to be 2 weeks, a

conservative estimate would be 30 days. This duration of exposure differs significantly from the duration of the toxicity study chosen by HIARC to be indicative of intermediate-term exposure. The endpoint of 1.8 mg/kg/day was based on estrous cycle alterations and LH surge attenuation in a 6-month Sprague-Dawley rat study. It is scientifically incorrect to be comparing a daily dose to the endpoint from a 6 month study. A toxicity study of a more appropriate duration should be used to assess this type of exposure.

It is highly unlikely that there would be any intermediate-term risks for homeowners and children coming into contract with atrazine-treated turf. Atrazine residues would be washed to the thatch and soil either by sprinkler-irrigation (which is common in the southeast) or rain, which is also common in the southeast during the months atrazine can be applied (October through April). In the event that intermediate-term dermal risks need to be assessed, a more appropriate toxicological endpoint should be used that better represents the duration of exposure. If turf transferable residue at 7 days after application is used to determine potential dermal exposure to children and adults, then an endpoint from a toxicity study of similar duration should be used.

HED Response:

The Agency recently revised the toxicity endpoint selection document for atrazine (HIARC Report 12/22/2000). In it, the Agency applies a short-term exposure duration of 1-30 days based on the length of time to the effects seen in both oral and dermal toxicity studies selected for short- and intermediate term exposures. Therefore, as was stated in the November 15, 2000 occupational and residential exposure assessment, most atrazine handler and all residential exposures are expected to be short-term in duration. For intermediate-term postapplication exposures, it is expected that no individual would consistently be exposed to average residues greater than those at DAT 7 for over 30 days. The text and tables have been revised to clarify this position.

30. Pages 39, 42, 44 and Tables 12, 13, and 14: Both the timing of an atrazine application with respect to re-entry activities and what re-entry activities actually occur need to be taken into account when assessing post-application exposure. Manual irrigating/moving of irrigation pipe and scouting are highly unlikely to occur in areas designated as fallow and roadsides (note rate should be 1 lb ai/A). Manual irrigation/moving of irrigation pipe do not occur in newly planted conifer forests; scouting in conifer forests is not a typical practice. Staking, topping, and training of Christmas trees do not take place for at least 3 months after an atrazine application; harvesting of Christmas trees takes place in November and December, almost 9 months after a potential atrazine application. The

atrazine label prohibits harvesting and transplanting of turf for 30 days following an atrazine application. Since atrazine is applied to kill weeds, it would not make sense to have workers hand-pulling weeds on golf courses or sod farms immediately following an atrazine application.

Based on this information, post-application exposure assessment is not required for fallow ground, roadsides, and conifer forests. The risk assessment for people staking, topping, training or harvesting Christmas trees should be removed as there would be no atrazine residues 3 or 9 months after application. The risk assessments for transplanting, harvesting and hand weeding golf course turf and sod farms should be removed. When the timing of atrazine applications are taken into account relative to re-entry activities, any post-application exposure concerns are alleviated.

HED Response:

Based on comments received and confirmed by BEAD and other authorities on agriculture, postapplication exposure to atrazine on fallow lands or CRP grasslands is considered unlikely, and even less likely in the short-term after spraying. Exposure of workers on treated highway rights-of-way or roadsides would probably be unlikely in the first week after spraying, but it is possible the public could be exposed for short durations. The Agency has no transfer coefficients specific for tractor mowing. As a whole, these exposures are considered to be negligible. The BEAD also agrees that hand weeding sod or turf is unlikely at any time, and harvesting unlikely in the short term after herbicide application. Irrigation of forests or tree farms is unlikely, but staking may be done at any time. The exposure and risk assessment has been updated to reflect these refinements.

31. Pages 43 and 44, Bullet Items: It is not scientifically valid to deliberately pick out the highest data point from a series of values. The purpose of taking multiple samples is to obtain confidence in the data, to see the distribution or variance of the data, and to obtain a measure of central tendency of the data. It is for these reasons that scientists take multiple measurements whenever possible. All data points collected at the time-point of interest (ie 0 DAT or 7 DAT) should be used to calculate a mean value which is then used in the calculation of daily dose. It is unclear why the data is being manipulated in this manner. Conservatism to bias exposure to the upper-end is found in the other parameters of the dose calculations - transfer coefficients and the assumptions of hours in contact with treated foliage.

HED Response:

The Agency has presented the MOEs using the average residues on each day after treatment, from each geographic application site. This provides

the maximum amount of information for the Risk Manager for this chemical. For the purposes of regulation, i.e., labeling, sometimes residues will be averaged from different test sites if there are not significant differences in initial dislodgeable residue levels or rates of dissipation. The atrazine residue data show considerable geographic variation, particularly in dissipation rate. For both the liquid and granular applications on turf, the DFR dissipation rates were considerably slower at the Georgia site. The exposure duration can be an under- or over-estimate depending on the crop, location, time of year, i.e. scouting vs. harvesting, so for large assessments such as this the Agency uses eight hours consistently. The transfer coefficients for each activity for each crop incorporate the ARTF study data received to date, and the values are selected to be central tendency from the full range of the relevant studies.

32. Page 120, Table 11: It appears that the dislodgeable residue values listed in this table are incorrect. For MRID 449588-01 (atrazine granular turf application), none of the values presented in this table agree with the actual study data from the referenced report. For example, 0 DAT GA should be 0.048, not 0.0585; O DAT FL should be 0.154, not 0.162. Please correct the numbers in these tables. Also, the data for the irrigated turf from the same study (MRID 449588-01) are not presented here – they should be included since the label requires the granular formulation of atrazine to be watered-in. Residential post-application exposure risk assessments should be calculated for irrigated turf as well as for nonirrigated turf.

The 12-hour residue for the NC liquid-treated turf appears to be unusually high when compared to the residue before and after this time point and when compared to the same timepoint at the GA site. Please verify that this is in fact the correct number.

HED Response:

The data from both turf transferable residue studies were re-analyzed using linear regression, which accounts for the minor differences between the values reported and those used in the exposure and risk assessment. The NC spray-treated turf had by far the highest residues, and all replicates at DAT 0.5 (12 hours) were consistently higher than at any other time. The DFR dissipation rates vary considerably between geographic sites for both the liquid turf application and the granular study. Without additional studies, these geographically distinct data should be included when calculating risk estimates.

33. Page 46, 6th Paragraph, Line 1; A lawn size of 0.5 acres (21,780 sq ft) is an overestimate of lawn size based not only on published data but as a function of practicality – finding a hose long enough to cover 0.5 acres for a hose-end

application would be almost impossible, number and location of faucets limit area treated, and time required to treat a half acre with a hose-end sprayer would be prohibitive for most people. A more typical lawn size is 6,400 sq ft (conversation with TrueGreen-ChemLawn, 1997).

A low-pressure handwand is a one-nozzle wand connected to a spray tank of 1 or 2 gallon capacity. The pressure used to drive the spray out of the nozzle is obtained by manually pumping a piston connected to the top of the spray tank. To accurately treat 0.5 acres with a low-pressure handwand would be impractical, Low-pressure handwands are used for treating small areas such as spot treatments in the lawn, ornamentals and shrubs, vegetable gardens, flower beds, and perimeters of buildings. An area of 1,000 sq ft is typically used for risk assessments using this type of equipment (same area used for belly-grinder). Table 16a needs to be revised using 1,000 sq ft for low pressure handwand (R2). This will change the MOEs to 5,488 for dermal and 508,200 for inhalation.

HED Response:

The use of 1000 sq ft for residential applicators using belly grinders is assumed, and use of a hand-wand for "spot treatment" would be limited to the same area. The revised exposure and risk assessment uses 1000 sq ft for the backpack and hand wand application by residents, assuming spot treatment use is more typical for these methods. Additional usage data, such as gallons used or acreage treated per day, could refine the current daily use rate assumptions and affect total exposure estimates. The Agency uses the Residential SOPs as the source for residential acreages applied, unless more specific information is available. The median lawn size is approximately 0.3 acres, while 0.5 acres is approximately the 80^{th} -90^{th} percentile, depending on the survey cited. Label instructions limiting use of the liquid formulation to spot-treatment would also help reduce the risk for low-pressure handwand and hose-end sprays as they would not be intended for application to an entire lawn.

34. Page 126, (Table 16a): Hose-end sprayer and push type spreader calculations utilizing PHED data should be deleted and replaced with the higher quality risk assessment using ORETF data.

HED Response:

See response to Comment #4.

35. Page 48, Handler Scenarios with Risk Concerns, 1^{st} Paragraph, Line 1: The statement that there are risks of concern for the hose-end sprayer and low-pressure handwand is incorrect and should be removed.

HED Response:

The exposure and risk assessment has been revised. See reponse to Comment #4.

36. Page 49, 7th Paragraph, Line 9: It is highly unlikely that there would be residential intermediate-term post-application exposure to treated turf given the high probability that a rain or irrigation event or a mowing event would take place within 7 days of an application. In the southeast, where atrazine is labeled for turf use, rain is quite likely to occur during the time period atrazine may be applied (October 1 through April 15). In addition, the consumer label recommends irrigation following application to increase efficacy of the product. Maintained lawns in the southeast are typically irrigated.

HED Response:

No intermediate-term residential exposures to atrazine are anticipated. The Agency evaluates the residential risk to the highest average post-application residues/shortest interval because residents cannot be restricted from accessing their lawns at any time. The highest atrazine residues were from spray applied by LCOs.

37. Page 50, 3rd Paragraph, Line 1:There are no wettable powder formulations available to the consumer; this needs to be corrected.

HED Response:

Only granular fertilizer and liquid formulations for hand spraying were assessed for consumers. The text has been clarified.

38. Page 50, 3rd Paragraph, Line 2: Data Sources for Scenarios Considered. Also, Page 55, Postapplication Exposure Risk Estimates: It is not scientifically valid to deliberately pick out the highest data point from a series of values. The purpose of taking multiple samples is to obtain confidence in the data, to see the distribution or variance of the data, and to obtain a measure of central tendency of the data. It is for these reasons that scientists take multiple measurements whenever possible. All data points collected at the time-point of interest (ie 0 DAT or 7 DAT) from all sites should be used to calculate a mean value which is then used in the calculation of daily dose. There is no statistical justification for not combining the data from the two test sites. It is unclear why the data is being manipulated in this manner. Conservatism to bias exposure to the upper-end is found in the other parameters of the dose calculations - transfer coefficients and the assumptions of hours in contact with treated turf.

HED Response:

See response to comment #31.

39. Page 50, 4th Paragraph, Line 3: The scenario of a child picking out 300 mg of granules from treated turf and eating them is not a viable scenario for granular atrazine. An NPIRS search on 12/07/00 for Federally Active Registrations for products containing atrazine shows that a true granular formulation of atrazine (without fertilizer) does not exist in the market place. There are many turf products where atrazine is coated on the fertilizer granules at varying low concentrations of less than 2 % active ingredient. These are classified as granular formulations in the database, but are really fertilizer granules with a coating of atrazine sprayed on their surface. This fertilizer is then applied by the homeowner at a given rate to his lawn to provide weed control and fertility at the required level.

The ingestion scenario assumes oral exposure of applied granules in sufficient quantities to deliver atrazine. This is not an appropriate assumption for fertilizer. These products can be highly alkaline (pH around 10) and contain high concentrations of nitrogen and phosphorus and potassium salts. Ingestion of more than a "taste" is highly unlikely considering the caustic nature of fertilizer. Therefore, the ingestion of granule scenario is not something that would happen and should be deleted. It is also important to note that fertilizer is hydroscopic and when subjected to humid conditions, it dissolves and is no longer available in the granular form. The atrazine is then in the thatch, not on the leaf surface, and not available as granules for picking up and eating.

HED Response:

The Agency recognizes that atrazine is supplied as a fertilizer with a maximum of 1.5% active ingredient by weight. The information supplied thus far from the Scotts Corporation, as noted in the November 15, 2000 residential exposure assessment, describes the home lawn formulations as having particles the size of "beach sand." This statement was sufficient to allow the Agency to *qualitatively* state the risk from incidental ingestion is less than if particles were larger. Prompt watering-in also reduces the risk of accidental ingestion and decreases the available residues, as shown by the granular TTR study data.

40. Page 129, (Table 18): The formula used to calculate hand-to-mouth exposure in footnote d is incorrect – it is missing the 50% efficiency of transfer from hand to mouth. As a consequence the MOEs should be increased by a factor of two.

HED Response:

Table 18 has been revised and corrected to reflect the current version of the Residential SOPs.

41. Page 53, 1st Paragraph, Line 4: The use of the default 5% of the application rate should be used in absence of compound-specific data. Since there exists TTR data for both the granular and liquid formulations of atrazine, the TTR data should be used. An evaluation of the limited data available (Clothier, 2000) to compare how much residue can be transferred from surfaces by dry hands versus wet hands indicates that the increase is 3-fold (see position paper at the end of this section); this is substantiated by proprietary work in progress by a task force. The work by Clothier also indicates that the PUF roller (a sampling technique similar to that used in the TTR studies) removes more surface residue than does a hand press, and thus overestimates potential transfer of pesticide from turf to hands. The average amount of residue transferred in the granular turf transferable residue study was 0.43% (non-irrigated turf) and 0.35% (irrigated turf). Multiplying these numbers by 3 results in 1.29% (non-irrigated) and 1.05% (irrigated) of the application rate for a "wet" hand transfer. These values should be used to assess potential "wet" hand-to-mouth exposure to toddlers. When these values are used, the short-term MOE is 1,300 (non-irrigated) and 1,600 (irrigated).

HED Response:

The Agency recognizes the work by Clothier and others. The data known to the Agency appear to support the transfer of approximately 1-5% of the applied chemical to hands wetted with saliva. Therefore the Agency uses 5% as the higher-end for incidental ingestion from finger licking where dislodgeable residue data (as opposed to TTR) are not available.

42. Page 54, 2nd Bullet Point, Line 6: The statement that the turf transferable residue study done with the liquid formulation was at 4.0 lb ai/A contradicts information in Table 11 (page 120) that states the application rate to be 2.0 lb ai/A. Please clarify.

HED Response:

The sentence:
"The granular and spray turf residue data which were submitted also use a 2.0 and 4.0 lb ai/acre, respectively, application rates." has been corrected to read: "The granular and spray turf residue data which were submitted also used a 2.0 lb ai/acre application rate."

43. Page 55, 4th Bullet Point, Line 3: The statement that the turf residues are greater on the day after application is not supported by the data from the granular TTR study (MRID 449588-01). At the GA site, the highest average residues were seen at the "0 hour" time point; at the FL site, the highest average residues were seen at 4 hours after application. Please revise or clarify this statement.

There has been no agreement by risk assessors to discard data from the day of application due to high variability; in fact, this data is critical to evaluating risks for people re-entering treated areas – especially in residential areas where a restricted entry interval is not typically feasible. When examining this type of data, there is no trend for day of application data to be any more variable than data collected at any other time point. This statement regarding the discarding of data is misleading and unsubstantiated; it should be removed from this document.

HED Response:

The description of the TTR data has been clarified. The statement implying general agreement as to which residue data are most variable has been removed from the document.

44. Page 55, 1st Paragraph of Post application Exposure Risk Estimates: There appears to be a mix-up here. The two short-term dermal scenarios that

result in MOEs less than 1000 are with the liquid-treated turf (see Table 17). This was based on using the NC-liquid data, not the Florida granular residue data. Please correct.

Since the dermal risks were summarized for the liquid formulation, it would be helpful to also summarize those for granular-treated lawns - the short-term and intermediate-term dermal postapplication MOEs are all above 1000.

As mentioned previously, when the TTR data is used and adjusted by a factor of 3 to account for wet hands, the hand-to-mouth risks are acceptable.

As mentioned previously, the ingestion of granules is not a viable scenario due to the caustic nature of the fertilizer.

HED Response:

The error cited has been corrected in the revised document.

45. Page 56, 1st Paragraph, Line 1:under Summary: It is not clear if the risk concerns are for the granular or the liquid formulations.

HED Response:

The statement has been clarified in the revised document to show the greatest postapplication risk estimates are for liquid formulations.

46. Page 56, 2nd Paragraph, Line 1: under Summary: The statement that applying a granular formulation and using the lawn the same day may cause an exposure concern for an adult is incorrect. As shown in Table 17, the postapplication MOEs for an adult are above 1000. Table 16b shows the MOE during application with a push-spreader are also above 1000. Please revise the statement.

HED Response:

The statement has been corrected in the revised document.

47. Page 63, Table 2: Note that the UF for dermal and inhalation risks is specified as 100; this should probably be changed to reflect the difference in uncertainty factors for residential versus occupational risks.

HED Response:

The UF has been clarified in Table 2 in the revised document.

48. Page 70, Table 4, Scenario 12: Lawn Handgun, Liquid Formulations: Note that this should state “LCO” not “PCO”. With respect to the ORETF data, the data generated for professional lawn care operators is based on mixing and loading and application. There were no significant differences between formulations mixed (15 replicates per formulation) and application only (30 replicates), thus one can combine all the dermal data for risk assessment purposes.

HED Response:

The document has been revised to clarify the difference between LCO and PCO.

Comments on the Use of a 5% Factor Applied to the Application Rate for Assessment of Hand-to-Mouth Exposure to Turf Treated with Atrazine

EPA has used a 5% factor in the atrazine human health risk assessment to reflect concern about increased exposure to pesticide residues during hand-to-mouth contact due to wet hands or sticky fingers. EPA has applied this factor only for exposure from hand-to-mouth contact. Additionally, EPA has applied this factor to the maximum application rate of atrazine to turf, rather than using the atrazine-specific turf transferable residue (TTR) data that was used in the dermal exposure assessment. The following presents information refuting the use of this factor in the atrazine assessment.

EPA has presented the Standard Operating Procedures (SOP) (EPA 1997a) used for assessment of non-dietary (residential) scenarios to the Science Advisory Panel (SAP) for peer review prior to their use for regulatory purposes. The SOPs were initially presented to the SAP in September 1997 and a revised version was made available in December 1997 (EPA 1997b) which incorporated comments from the SAP. In September 1999, additional revisions and issues regarding the SOP factors were presented to the SAP (EPA 1999a). The factor being discussed herein was discussed briefly in the revisions presented in September 1999 (EPA 1999a) and in the SAP final report (EPA 1999b). Based on a review of the SAP background document, references listed in the background document, and the SAP final report from the September 1999 meeting, it can only be said that the conclusions were equivocal.

The background document for the SAP report proposes the use of the 5% as: “In the absence of chemical specific transferable residue data on turfgrass, the Agency recommends dislodgeable values of 5 percent for use in post-application dermal exposure estimates in the Residential SOPs.” (page 25, EPA 1999a, emphasis added). It should be noted there are two important issues: 1) the absence of chemical specific data; and 2) use for dermal exposure. First, there is chemical-specific data for atrazine. It shows the turf transferable residue to be around 0.4%

for the granular formulation. Secondly, nowhere in the background document or the final SAP report is the oral exposure scenario discussed in relation to sticky fingers or wet hands transferring additional residues.

EPA references a variety of sources in the SAP background document and during discussions with atrazine registrants to support the proposal of a 5% factor applied to the initial application rate (Clothier 2000; Camann et al. 1995; and Lu and Fenske 1999). The report by J. Clothier (2000) presents a 2.5-3.5 times higher transfer efficiency for wet palms versus dry palms. Camann et al. (1995) and Lu and Fenske (1999) observed that using moistened materials for dislodging residues resulted in less that 5% transferability (0.6 to 2.1% and 1 to 3.1%, respectively). Additionally, these references present data that show that the hand press method of transferring residues gives much lower transferability than methods used in TTR studies. Thus, the data from the atrazine turf study is already conservative as it was conducted using a modified cloth roller method. Finally, these references also support that dislodgeability is greatest from vinyl (the source of the Clothier data) compared to carpet or turf, so applying data from vinyl to a turf analysis is even more conservative.

“Sticky fingers” or wet hands are only discussed in the “indoor surfaces” section of the final SAP report, not in the section pertaining to turfgrass. The final report states, “With respect to moist or sticky hands, there are not enough available data to make a determination whether using a higher “percent transferable residue” factor is justifiable.” (page 11, EPA 1999b).

Finally, the use of the 5% factor is arbitrary and has not been used consistently by the Agency. EPA staff have stated that this factor was used in other assessments of exposure to organophosphate products on turf. A review was conducted of the risk assessments currently available to the public on the Internet at the EPA-OPP website. The following conclusions can be made:

- The factor was used in the REVISED malathion assessment for defense of the mosquito-spray scenarios where no TTR data was available. This is an appropriate use of the factor.

- The factor was NOT used in the acephate assessment, instead TTR data was used. This is an appropriate use of TTR data and the factor is unnecessary.

- The factor was NOT used in the bensulide assessment, instead TTR data was used. This is an appropriate use of TTR data and the factor is unnecessary.

In summary, the use of the 5% factor has not been adequately peer-reviewed and a review of the data on the effect of wet palms does not support the use of this factor. It is appropriate to use chemical-specific data, without application of additional

factors, when they are available (i.e., TTR data). However, if EPA continues to believe that a factor for wet hands must be included a full peer-review of the data should be conducted.

HED Response:

This is not an error correction comment. See response to Comment # 41.